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POSSIBLE CONSEQUENCES OF AN INCREASED MUTATION RATE[1]

JAMES F. CROW
University of Wisconsin

This is the third article in a series on Genetics and Radiation.

IN AN EARLIER ISSUE OF THIS JOURNAL I have presented estimates of human mutation rates and the amount by which they might be increased by radiation (1). The present article is an attempt to assess the effects of such an increase on the population.

I should like to start by reemphasizing what was stated earlier, that estimating overall human mutation rates, and particularly the estimation of radiation effects involves many unprovable assumptions. The data, even from experimental organisms, are frequently inaccurate. To this is added the still greater uncertainty of extrapolating from experimental organisms to man. Finally, in discussing the consequences for man of an increased mutation rate there are the difficult problems of deciding by what criteria radiation damage is to be measured.

For all these reasons, any sort of quantitative assessment of radiation mutational damage is a dubious undertaking. In fact, Neel and Schull (2) in discussing the difficulties involved conclude that "semi-quantitative treatments are ill-advised, since except to the relatively few who have made a detailed study of the problem, they impart an air of mathematical exactitude and scientific accuracy to an area where the errors are sometimes large and often indeterminate." However, my opinion is that a poor and provisional estimate is better than no estimate at all, provided that we keep always in mind the possibility that it may be grossly in error.

A General Principle of Genetic Damage Due to Radiation

Almost all mutations, and in particular radiation-induced mutations, that have an effect large enough to be measured are harmful in some way. This is an observed fact in experimental animals, but it is also to be expected on theoretical grounds; mutations, being essentially random changes, are much more likely to be harmful than beneficial. We can state, as the National Academy of Sciences Committee on Genetic Effects of Atomic Radiation (3) did, that "Complexities notwithstanding, the genetic damage done, however felt and however measured, is roughly proportional to the total mutation rate." A second fact is, that at the low dosages likely to be encountered in the human population, the number of mutations induced is strictly proportional to the amount of radiation, irrespective of the intensity or spacing of the dose. Combining these two statements we conclude that the amount of genetic harm done is strictly proportional to the radiation dose. The evidence for this statement is given in non-technical form by Muller (4).

[1]Paper number 656 from the Department of Genetics.

This tells us something, but not enough. It says that $50r$ of radiation causes 5 times as much harm as $10r$, but it doesn't say how much either causes. In the following sections some quantitative estimates will be given. But first it is necessary to consider some general principles governing the fate of mutant genes in populations.

The Haldane-Muller Principle

The basic quantitative relation between mutation rate and the amount of genetic damage was first pointed out by Haldane (5). Essentially the same idea was used independently by Muller (4, 6, and earlier papers) as a basis for assessment of possible mutational damage from radiation. I think it is instructive to consider the problem both ways.

Haldane expressed the mutational damage in terms of the *fitness* of the population. Fitness is used in a strictly Darwinian sense, *i.e.*, the ability to survive and leave descendants. Consider a mutant gene that lowers the fitness of the heterozygous individual carrying it by a fraction s. For example, if s is .05, individuals carrying this gene will be represented next generation by only 95 per cent as many descendants as if they did not carry it. Such a mutant gene will persist in the population an average of $1/s$, or 20 generations (6).[2] Now suppose that the normal gene has a probability of m of mutating each generation. Then in each generation the proportion of individuals carrying newly mutated genes at this locus will be $2m$. The factor 2 comes from the fact that each individual has 2 sets of genes. If the mutant is harmful it will be so rare that reverse mutation can safely be ignored. Since each mutant persists an average of $1/s$ generations, the population will eventually contain an average of $2m/s$ mutant genes per individual. But the effect of each mutant gene is to decrease the fitness by a fraction s. Hence the average reduction in fitness of the population is $(2m/s)s$ or simply $2m$. The remarkable result is that the s factors cancel out; the effect of mutation on a population is proportional to the mutation rate, but is independent of the effect of the mutant on the individual. Considering mutants at all loci, if they act independently and are rare relative to normal genes, the effect is approximately the sum of the individual effects. We can thus state the Haldane principle as follows: The fitness of an equilibrium population is decreased because of mutation by a fraction approximately equal to M, the total mutation rate. M is the total rate per diploid individual, *i.e.*, twice the gametic (haploid) rate.

Muller has measured mutational damage in terms of *genetic deaths*. A genetic death is the extinction of a gene lineage through the premature death or reduced fertility of some individual bearing the gene. Consider a large population whose size remains constant from generation to generation. If it starts out with a certain number of harmful mutant genes, this number will decrease each generation since the carriers of the mutant have a smaller chance of surviving and reproducing. This process will continue until all the mutant genes are eliminated. Table 1 illustrates that, irrespective of the value of s, each mutant eventually leads on the average to one extinction.[3] Of course some mutants will increase in number by chance, but this will be exactly compensated on the average by those that are lost by chance. We can state the prin-

[2] If this statement is not self-evident, consider the following argument. If the initial fraction of mutant genes is g, the fraction in successive later generations will be gw, gw^2, gw^3, . . . , where $w = 1 - s$. The total number of individuals carrying the mutant for all time is $g + gw + gw^2 + gw^3 + \ldots$ But $g(1 + w + w^2 + w^3 + \ldots) = g/(1 - w) = g/s$. Dividing this by g, the initial fraction, gives $1/s$ as the average number of times a mutant is expressed before it is eliminated.

[3] More formally, the fraction of mutants eliminated the first generation is s_1, in the second generation is $(1 - s_1)s_2$, in the third $(1 - s_1)(1 - s_2)s_3$, and so on. Letting $w_i = 1 - s_i$, the total fraction of eliminations is $(1 - w_1) + w_1(1 - w_2) + w_1w_2 - w_1w_2w_3 + \ldots = 1$. So each mutant leads to an average of one elimination, irrespective of fluctuations in s.

TABLE 1

Numerical examples illustrating the principle that each harmful mutation leads eventually to one genetic death. In each case there are 1000 new mutant genes to start with. The total population is assumed to remain constant from generation to generation and to be large enough that the mutants constitute only a very small fraction. Mutants reducing the fitness by .8, .2, and by a variable amount are assumed. In each case the number of eliminations, or genetic deaths, eventually totals 1000.

	$s = .8$		$s = .2$			s variable	
Generation	Number of remaining mutants	Number of mutants eliminated	Number of remaining mutants	Number of mutants eliminated	s	Number of remaining mutants	Number of mutants eliminated
0	1000		1000		.2	1000	
		800		200			200
1	200		800		.25	800	
		160		160			200
2	40		640		.33	600	
		32		128			200
3	8		512		.25	400	
		6.4		102.4			100
4	1.6		409.6		.50	300	
		1.3		81.9			150
5	0.3		327.7		.10	150	
		0.2		65.6			15
6	0.1		262.1		.00	135	
		0.1		52.4			0
7	0.0		209.7		.50	135	
		0.0		41.9			67.5
8	0.0		167.8		.50	67.5	
		0.0		33.6			33.8
9	0.0		134.2		.10	33.8	
		0.0		26.8			3.8
10	0.0		107.4			30.4	
∞	0	0	0	0		0	0
Eventual Total	1250	1000	5000	1000			1000

ciple as Muller has: each harmful mutation leads on the average to one genetic death.

These two formulations, though similar in many ways, have some important differences, both in assumptions and in conclusions. The Haldane calculations are based on the assumption that the population is in equilibrium and measures the loss in fitness in a single generation due to the accumulation of mutations that have occurred previously. The Muller formulation makes no assumption that the population is at equilibrium, only that the number of mutant genes is a small fraction of all genes and that the population size remains stable. If the population is expanding, the number of genetic deaths increases proportionately. This principle gives the total genetic damage to be expected in the future from mutant genes now present.

Though the two approaches differ, the same general principle emerges. Whether the damage is measured as loss of fitness in an equilibrium population or as future genetic deaths, *the total mutational damage is equal to the total mutation rate.*

The foregoing theory assumes that the mutants have a harmful effect in the heterozygous condition, and that homozygous mutant individuals are so rare that they can be neglected. The most frequent mutation in Drosophila is a detrimental "recessive," but careful tests usually reveal that the mutant has an appreciable effect on viability when heterozygous. For example, the average mutant that is lethal in the homozygous condition causes about 4-5 per cent pre-adult deaths when heterozygous. If adult mortality and decreased fertility were considered, the heterozygous effect on fitness would probably be greater. It is probable that the same absence of complete

dominance is also characteristic of mutants that cause only slight damage when homozygous, but this point has not yet been established experimentally. Any mutant gene that has a measurable harmful effect when heterozygous will usually be eliminated from the population before it ever has a chance to become homozygous.

It is quite safe, I believe, to ignore in this discussion mutations classed as dominant lethals in experimental animals and plants. These are mostly due to gross changes in the chromosomes. At the low radiation dosages likely to be encountered in human populations, these would be very much less frequent than "point" mutations. Another reason is that any that do occur are likely to cause mostly very early embryonic deaths, which are of less consequence for human welfare than mutations causing disease or death at later stages.

The Haldane-Muller principle does not apply to genes that are maintained in the population in a balanced polymorphic condition, by heterozygote superiority or for other reasons. An increase in mutation rate at such loci does not cause a proportional reduction in fitness. The possible importance of such factors in non-inbred populations has been stressed by several authors (*e.g.*, 8, 9). But, although such loci may possibly account for a large fraction of the population variance in fitness, it is likely that this comes from a relatively small number of chromosome loci that individually, because of their polymorphism, make a disproportionately large contribution to the population variance (8). If the number of such loci is relatively small, they account for a small fraction of new mutants. Furthermore, the range of possible mutant types must far exceed the number of alleles maintained in balaneed polymorphism, and many of these mutant types, especially radiation-induced, may be unequivocally harmful. In any event the lethal and distinctly deleterious mutants studied in Drosophila which form the basis for most estimates of total mutation rate are of a type to which the Haldane-Muller principle applies.

There also may be genes whose effect on fitness is very slight. Perhaps the "polygenes" that determine quantitative characters are of this type. If the harmful effect of a mutant is of the same order as the mutation rate (say less than 10^{-4}) the Haldane-Muller principle does not hold exactly. However, such genes probably contribute relatively little to the total mutational load.

We are left then with the belief that the mutational load is due primarily to detrimental recessive genes that have small but not negligible effects as heterozygotes. Usually these cause no obvious visible abnormality. The kind of mutants studied in Drosophila and from which the calculations given in the earlier paper (1) were made are of this type. Since these mutants usually never become homozygous, it is their heterozygous (*i.e.*, dominant) effects that count. Therefore a simple theory, such as I have presented, based on only dominant mutations is probably a close approximation to the truth.

This theory, simple and direct though it is, is unsatisfactory from the standpoint of assessing human damage. For, although fitness is one aspect of the human population, it is not the most important one. What we should like to know is the amount of mutational damage in successive generations in terms of death rates at various ages, increased incidence of physical and mental disease, increased frustration and unhappiness — in short, the sum total of human misery. However, the total impact of mutation on mankind in such terms cannot be measured by any means now known. We can hope to estimate the increased frequency for specific genetic diseases. But even when this has been done for all known hereditary diseases only a small fraction of the total genetic damage will have been included; for most of the genetic damage, if we can analogize from Drosophila, is due to genes that cause a slight reduction of life

expectancy, a decrease in fertility, an increase in various kinds of ordinary illnesses, and other such non-specific effects. Measurement of the effect on fitness or of the number of genetic deaths at least has the merit that it is an approach to the *total* genetic damage. Intangible as it is, measurement of mutational damage in these terms gives some quantitative notion. But one must remember that a "genetic death" is not necessarily a physical death and that not all genetic deaths are equal in their impact on man's welfare. A genetic death resulting from early embryonic death or failure to reproduce may cause little or no distress. At the other extreme is a mutant gene that causes its bearer great pain or unhappiness, but which has very little effect on early death rate or fertility, and which therefore may affect many generations of descendants before its elimination.

The Effect of Changing Mutation Rates

The Haldane principle depends on the assumption of equilibrium between mutation and selection. I shall now consider some of the effects of departure from equilibrium.

Figure 1 is intended to show the effect on an equilibrium population of a permanent increase in the mutation rate. If the mutation rate is increased by a certain factor, X, the mutational load (measured as decreased fitness, or increased number of genetic deaths) gradually rises and approaches asymptotically a new equilibrium where the loss in fitness is X times as great. Although the final equilibrium value is independent of the harmfulness of the individual mutant, the rate at which the population approaches the new equilibrium is strongly dependent on it. The rates have

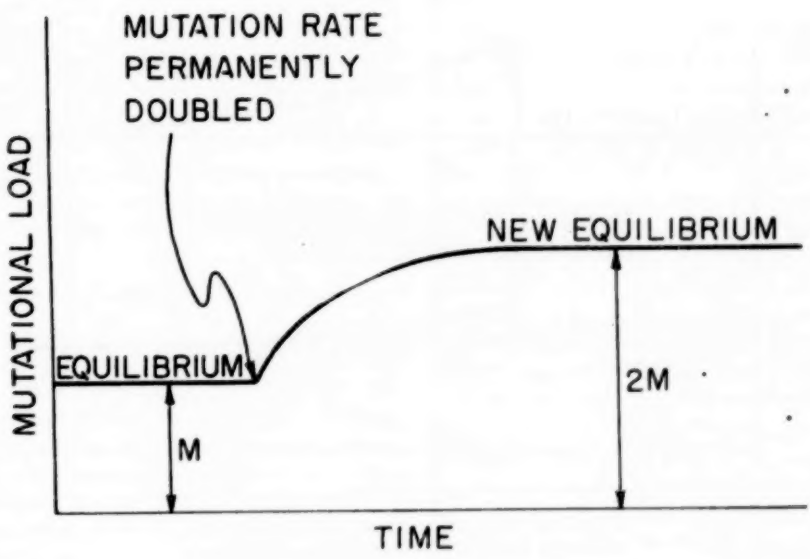

FIGURE 1. Effect of a permanent change in mutation rate on the mutational load.

been studied by Wright (10, and unpublished).

If the mutation has a completely lethal effect, the new equilibrium is reached in one generation. But many mutations of great overall consequence for man probably have relatively small individual effects on fitness. For these it is convenient to compute a quantity analogous to the half-life of radioactive substances. This is the number of generations or years required for the fitness of the population to be changed half way to the new equilibrium value.[4] A few numerical values are given in Table 2.

TABLE 2

Values of the time, T, required for the population to move half way to a new equilibrium when the mutation rate is changed, for different values of s, where s is the proportional reduction in fitness caused by the mutant. T is also the time when the mutations occurring in a single generation will have caused half of their total harm to the population. In converting from generations to years, an average time of 30 years is assumed.

	T	
s	Generations	Years
.25	2.8	84
.10	6.9	207
.05	13.9	417
.01	69.3	2079
.001	693.1	20793

Figure 2 is intended to illustrate a different situation, one where there is only a single generation of increased mutation rate followed by a return to normal. The upper line shows the equilibrium number of mutant genes per individual, M/s. This equilibrium is maintained as long as the new mutations are exactly balanced by elimination of old mutant genes. When the mutation rate is doubled for one generation, M new mutant genes per individual are added to the population. The number then gradually decreases to the old equilibrium value.

The lower line in Figure 2 shows the mutational load. The effect of the single generation of increased mutations is spread

[4]For moderately small values of s the number of generations required to go half way to the new equilibrium is very closely approximated by $(1/s)\log_e 2 = .693/s$.

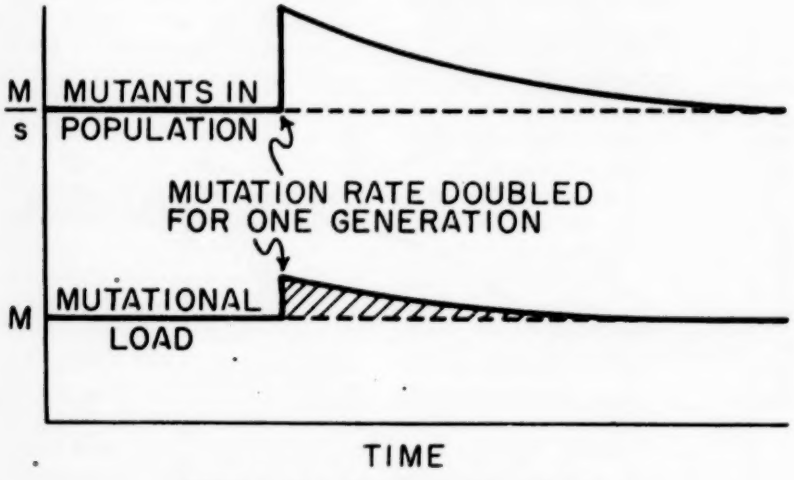

FIGURE 2. The effect of an increased mutation rate for one generation on subsequent generations. The upper line gives the number of mutant genes per individual in the population, the lower the mutational load. The ratio of these two stays constant throughout the process.

over many generations in the future. But the total increase in the load, the shaded area in the graph, is exactly equal to M, the number of added mutations.

In inquiring as to how long a time the effect of the mutation increase persists, a meaningful quantity is the "half damage time." This is the time by which half the total damage due to these mutations will have taken place. The half damage time is the same as the time for the number of mutants to return half way to their equilibrium value.[5] Thus a mutant gene that causes a 10 per cent reduction in fitness will exert 50 per cent of its total harm on the population in about 7 generations, irrespective of how this harm is manifested or measured.

The new mutations are, of course, a heterogeneous group with varying effects on fitness. The approach to equilibrium is a complex composite of the varying rates of approach of the individual mutants. In the earlier generations this is relatively rapid because of mutants having large effect, but later as these are eliminated and mutants with small effect become relatively more important the approach is very slow. For example, if the new mutants consist of 25 per cent with $s = .04$, 25 per cent with $s = .02$, and 50 per cent with $s = .01$, the average persistence is about 70 generations, but 50 per cent of the total genetic damage occurs in about 40 generations.

Effect of a Change in Environment

A major difficulty with the foregoing theory comes from the fact that in the human population many of the factors that determine the equilibrium are changing faster than the equilibrium is approached. The environmental improvements of the last few centuries have undoubtedly had a great effect in decreasing the harmfulness of many mutants. A mutant that caused a high probability of death a century ago may have a minor effect now. In so far as an improvement in environment ameliorates, rather than completely obliterates, the harmful effect of a mutant the Muller principle still holds. For example if a mutant which previously caused its bearer to have a 50 per cent probability of death in an improved environment causes only a 10 per cent probability of death, it still leads to one genetic death, but the effect is spread over 5 times as many generations.

Figure 3 is intended to show the effect of an improvement in the environment on a population previously at equilibrium. The improvement is assumed to be permanent. Following the changed environment, the mutational load drops suddenly in proportion to the magnitude of the change in fitness effected by the improved environment. Then the population slowly returns to its previous position. Each successive new improvement causes a similar drop. Contrariwise, any return to the original conditions after the improved situation increases the load.

The present human population, especially in the technologically more advanced countries, may be considerably out of equilibrium in this respect. The population is probably at a stage where current eliminations are insufficient to balance the past and current mutation rates. If the present environment can be maintained (but is not further improved), the population will eventually return to a state where the number of genetic deaths per generation is equal to the number in the past. Thus the current generations are probably enjoying a respite. But the harm is postponed rather than prevented entirely, unless the environmental change is such as to render a previously harmful gene completely innocuous. There will be future improvements in the environment, probably much more spectacular than those of the past. The continued postponement of genetic deaths demands continuous new improvements of the environment, but whether such im-

[5]Since half as many mutants will do half as much total damage, when the number of mutants has been reduced by half, half the damage will have been done.

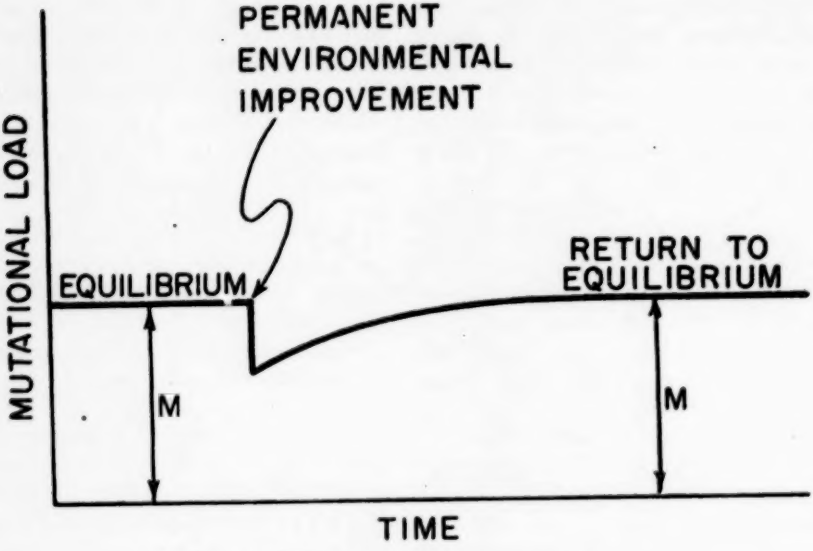

FIGURE 3. The effect of a permanent improvement in the environment on the mutational load. Each new improvement would cause a similar drop, followed by a slow return to the earlier condition, unless the environmental change is such as to render the mutant *completely* innocuous.

provements can keep ahead for long times in the future is a question about which one can only guess.

As emphasized earlier, what we are primarily interested in is not reduction in fitness *per se* but the associated increase in human misery. From the standpoint of long-time human welfare, the most beneficial kind of environmental advance is one that reduces the amount of suffering associated with a mutation by a greater fraction than the fitness is increased. On the other hand, if the fitness is greatly increased but the amount of suffering not reduced correspondingly, the long-time total misery will increase.

The Possible Effects of an Increased Mutation Rate on the Survival of the Population

In one respect the theory developed in the previous sections is directly applicable. Since the population fitness is a measure of its ability to survive and reproduce, any phenomenon that changes the fitness will be directly reflected in this ability. We may therefore inquire into the possibility that an increase in mutation rate may reduce the fitness of the population to such a point as to seriously threaten its survival. At a time when overpopulation is a major deterrent to economic advance in much of the world and a potential threat to human welfare everywhere, this may seem like a peculiar question to raise. Nonetheless a high enough mutation rate could lower the survival and reproductive powers of the population so that it might not be able to maintain itself. Is such a possibility at all likely?

The total (diploid) rate of mutation to appreciably harmful genes in man has been estimated, with a great deal of uncertainty of course, as perhaps as high as .30 (1, 7, 9).

That is, 100 persons would carry a total of 30 new mutations. This means that if the population is now maintaining its numbers by producing an average of two offspring per parent, a population with no mutational impairment would survive and reproduce at such a rate that 30 per cent premature death or sterility would still leave an average of two offspring per parent. A doubling of the mutation rate would mean that, after equilibrium is reached, the population must have sufficient survival and reproductive capacity that perhaps 60 per cent deaths could be tolerated. The number would actually be somewhat less because of coincidence of mutants in the same individual.

In the most fertile human populations, such as the Hutterites and some rural populations in Quebec where high conception rates are combined with favorable living conditions, the total number of children per family is 10 or more. This is five times the replacement rate so 80 per cent deaths could be tolerated in these populations. It is clear that the *potential* reproductive capacity of the human population is sufficient to permit an increase of several fold in the mutation rate for several generations. The problem of actual survival would begin to become critical only after many generations as the equilibrium state is approached.

To state that the human population could stand a several fold increase in mutation rate without a threat to persistence from decrease in survival and reproductive potential *per se* is of course not to state that such a change would not have disastrous effects on the population for other reasons. For one thing if the number of genetic deaths were greatly increased there would be a corresponding increase of all illness and incapacitation of genetic origin. In a system of careful cost accounting, the unhappiness, suffering, or inefficiency of the well caused by their having to care for the physically or mentally sick should be charged to the mutational load. In such a sense the mutational load may extend to persons who do not actually carry a mutant gene.

Despite the complexity of human society and the limited applicability of the simple analysis followed here I believe it is safe to say that the human population is not likely to encounter any amounts of radiation that would exert enough of an effect on survival and reproductive capacity to be a serious hazard *for this reason alone*. Even one generation of exposure to a near lethal dose would probably not lead to population extinction for the effects would be spread over many generations. In particular, if the population stays within the 10*r* limit recommended by the National Academy of Sciences Committee (3) and the National Committee for Radiation Protection, it is safe from the survival viewpoint.

Attempts to Estimate the Magnitude of the Impact of 10*r* of Radiation in Various Ways

Table 3 gives some crude estimates of the amount of genetic effect to be expected from 10*r* of radiation (the amount recommended as the maximum average gonad dose for the population) as a single generation indefinitely in the future. The first estimate is for a single dominant mutation which, being highly debilitating, is transmitted to a second generation only in a minority of cases. Thus most of the impact is in the first generation. The second is a more inclusive category intended to include all of the more severe impairments thought to have a clear hereditary origin. Next are infant and childhood deaths based on human death rates from consanguineous marriages. These include stillbirths and deaths at all childhood ages up to sexual maturity. The fourth category is an estimate of embryonic and infant deaths, based on total deaths in mice during embryology and for the first 3 weeks of post-natal life. Finally the total "genetic deaths" are estimated, based on radiation-induced mutation rates in mice.

TABLE 3

Crude estimates of the effect of 10*r* of radiation on the human population. The first two columns give the effect of the first generation. The last two columns can be interpreted either of two ways: (1) as the total effect for all time in the future from a single dose assuming constant population size, or (2) the effect in a single generation after a population has received 10*r* per generation for a large number of generations. All of these estimates depend on mouse data for radiation-induced mutation rates, and on other data which are not always accurate. Therefore, the numerical values should be regarded only as roughly indicative.

	First Generation Effect		Total Effect	
	Cases as a fraction of total population	Number of cases in a population of 100 million	Number of cases as a fraction of total population	Number of cases in a population of 100 million
(1) Achondroplasia	0.000005	500	0.000006	600
(2) Gross mental or physical defect	0.0004	40,000	0.004	400,000
(3) Infant and childhood death	0.001	80,000	0.02	2,000,000
(4) Embryonic and early childhood deaths	0.002	200,000	0.04	4,000,000
(5) Total "genetic deaths"	0.003	300,000	0.05	5,000,000

The figures in Table 3 were obtained as follows:

(1) *Effect on specific diseases.* With a disease due to a single dominant gene, the effect of an increased mutation rate will take place immediately. With a recessive sex-linked gene about a third of the mutations will be expressed in the first generation, and the rest will make their first appearance over the next half-dozen generations. But with an autosomal recessive mutant the proportion that will be expressed in any one generation is extremely small, usually less than 1 per cent and often much less.

The example chosen is a dominant mutant, achondroplasia. This is an example of a highly deleterious dominant gene, and most of the total impact of the mutation is on the first generation (11). The reduction in fitness of persons carrying this gene is estimated to be about 4/5. To estimate the number of mutations induced by 10*r*, I have taken the rate for mice, which is about 2.5 mutations per million genes for 10*r*. On this assumption, if each parent received 10*r* there would be 5 new mutations per million progeny. The average persistence of this mutant is about 5/4 generations, so the eventual number of cases would be about 625 per 100 million.

If the X-ray mutation rate is correlated with the spontaneous rate, this probably represents an underestimate, for achondroplasia is one of the most frequently occurring spontaneous mutations. A detailed discussion of this disease is given by Penrose (8, p. 93).

(2) *Gross mental or physical defect.* Roughly 5 per cent of the children born have some gross mental or physical defect and geneticists have estimated that perhaps half of these have a simple genetic origin (3). I shall take the figure as 2 per cent. A dose of 30-80*r* produces a mutation rate in mice that is equal to the spontaneous rate in man (3, 11). I shall assume 50*r*, so 10*r* is 1/5 this amount. If this figure is used, then $1/5 \times .02$, or .004 would be the eventual increase in such defects due to continued exposure to 10*r*. Since a substantial fraction of such conditions in man follow a simple dominant pattern of inheritance, I have assumed that 10 per cent of the total effect would appear the first

generation or 40,000 cases per 100 million births.

(3) *Infant and childhood death.* This calculation uses the increased death rate from birth (including stillbirths) to early adulthood among the children of consanguineous marriages as an estimate of the amount of hidden genetic damage. Using this, and assuming that the amount of heterozygous expression of recessive genes is the same in man as for lethal factors in Drosophila, one can calculate the increased death rate to be expected from this cause in non-inbred families. This calculation led to a value of 6 to 10 per cent (12); I shall use .08. A further assumption is, as in the previous paragraph, that 10*r* is 1/5 the amount of radiation required to double the human mutation rate. This gives 1/5 $\times$ .08 = .016 as the total damage. Drosophila data give 4-5 per cent as the amount of heterozygous expression. Allowing for a few dominant mutants during this time, I shall assume that 6 per cent of the total effect, or .00096 occurs the first generation.

(4) *Embryonic and infant deaths.* This estimate uses data from Russell (13) showing that female mice mated to males who have received 300*r* of X-rays had a 3-4 per cent reduction in litter size. The litters were counted at 3 weeks, so the figure represents the sum of embryonic and early post-natal deaths. For an exposure of 10*r* to *both* parents the fraction of first generation deaths is estimated as 20/300 of .035 or .0023. In order to compute the total damage it was assumed as before that 6 per cent of the damage occurred the first generation, giving .038 as the total.

(5) *Total "genetic deaths."* The average of several gene loci studied in mice gave 0.000,0025 mutants per gene for 10*r*. In Drosophila the ratio of all detectably harmful mutations to the single gene rate is about 10,000. Using this combination of mouse and Drosophila data we estimate for the number of mutations induced by 10*r*, .000,0025 $\times$ 10,000 $\times$ 2 or .05. The factor 2 comes from the assumption that both parents are irradiated. This .05, or 5 million in a population of 100 million, represents the total mutations or, by the Muller principle, the number of genetic deaths. Assuming as before that the first generation effect is 6 per cent, the estimate for this is .003.

Despite the limitations of accuracy and the tenuous assumptions that have been made, these figures are in reasonable agreement. They are to a large extent independent, but in one very important respect they are all subject to the same possible error. *All depend on mouse data for the rate of radiation-induced mutation.* Until there is quantitative information on man this is the best we can do, but this limitation must be kept in mind. There are of course other sources of error, but this is perhaps the greatest source of uncertainty.

Categories (3) and (4) are necessarily overlapping in that both include stillbirths and early childhood deaths (or whatever in man corresponds to mice less than 3 weeks old). None of these figures measure effects on fertility, for even the Drosophila data that go into the calculations of the total genetic deaths do not include this. Nor are the effects of mutants with very small effects included. In this respect the last row of figures are underestimates.

Assuming for the moment that these estimates are all entirely reliable, there are still difficult problems of interpretation. Which is more important, 40,000 physically or mentally defective or 200,000 embryonic and early childhood deaths. And how does either of these compare in its impact on mankind with 300,000 "genetic deaths"? Clearly some persons will find one measure more meaningful, other persons will prefer other measures. Some prefer a tangible estimate of known genetic disease. Others prefer an estimate of the total effect, even if intangible.

The general conclusions that emerge from the figures in Table 3, it seems to me, are as follows: unless the estimates given here are grossly in error, the figure of 10*r*

that has been recommended appears to be a reasonable one, "not harmless, mind you, but reasonable" (3). The amount of damage to be expected from one generation of exposure to this amount of radiation, though not negligible, would be a small fraction of the total human misery due to other causes. Long-continued exposure to this dose would cause more damage of course. Present estimates suggest that the long-time effects would still be considerably less than those caused by other factors, including spontaneous mutations. We can also hope that before many generations are exposed to this or any other level, the amount of knowledge will have increased so that better estimates can be made and public policy corrected accordingly

The above paragraph should not be construed to mean that an average gonad dose of 10*r* is harmless. Any amount is harmful to some extent, and every preventable instance of disease or death is one too many. Therefore, any reduction of the radiation exposure to the pre-reproductive gonads is a genetic gain. Fortunately, there are many ways in which such exposure can be reduced without impairment of economic development or the quality of medical diagnosis.

Evolutionary Considerations

A question which frequently arises is this: if, as is generally believed, mutations constitute the raw material for evolution, might it not be true that an increased mutation rate would increase the opportunity for further human evolution? I think there are two kinds of answers.

The first is that it is not easy to determine the optimum rate of mutation for evolution of any species. In man one can only guess. It is at least as likely that man's mutation rate is already too high for maximum evolutionary progress as that it is too low. See Muller (6) for a discussion.

The second, and to me more important answer, is that our main concern is not with the next million years of man's future (if he has that much of a future) but with the next few generations. For the foreseeable future, an increased mutation rate would only add to human misery. Radiation-induced mutations are at least as harmful on the average as spontaneous mutations, and there are reasons for believing that they are more so. Therefore any concern for the "short-term" genetic future, which is really a much longer time than we usually try to plan for in human affairs, would dictate that the mutation rate be kept as low as possible.

Much of the hope for man's future does not lie in biological improvement but in cultural, social, and scientific advance. And in the realm of the strictly biological, there is plenty of opportunity for selection among the array of genes already in the population.

Needed: Alternatives to Natural Selection

A few generations ago less than half of the infants born survived to maturity; now the majority do. This does not necessarily mean that natural selection was more effective then than now, for the efficiency of selection depends on how closely the differential survival and fertility are related to the genetic makeup. The chances are that many deaths and failures to reproduce were purely random with respect to genotype and therefore were a waste as far as human progress is concerned (except as Muller (14) points out, in so far as they prevented the world from becoming overpopulated even sooner). But some of the deaths and reproductive failures were selective and whatever genetic merits the human species now has it owes to this process, crude as it was.

We are approaching a stage when almost every zygote can grow into a potentially reproducing adult. Environmental advance may in this fashion largely eliminate natural selection as a moulding force. The chief selective factor may then become differences in desire for children. Deleterious

mutants are probably already accumulating in the population more rapidly than they are being eliminated, and any increase in the mutation rate will accentuate this.

In the realm of future possibilities there are at least three things than can perhaps be done to ameliorate the problem of accumulating deleterious mutations. One possibility lies in the reduction of not only radiation-induced but spontaneous mutation rates. This, of course, will not help reduce the number of mutants already in the population but will slow down the rate of addition of new ones. For example, the mutagenic activity of X-rays can be reduced by lowering the oxygen content of the tissues. So far the method is not practical for human use, but there is hope that at least some reduction of the genetic effects of radiation may some day be attained. On the other hand we have hardly any idea about what chemicals are mutagenic in man, and it is entirely possible that some substances among the variety of chemicals used in our present society are mutagenic. They may be a more serious problem than radiation. The most hopeful finding is that of Novick and Szilard (12) that some substances *decrease* the spontaneous mutation rate in bacteria. It may be a long time before any control over human mutations comes from this discovery, but it points the way to what may some day be possible.

Another thing that might be done is to continue *permanently* to improve the environment. We can and undoubtedly will continue to produce spectacles, hearing aids, insulin (though this may eventually be supplanted by transplanting pieces of pancreas), and hormones. We can also share a larger fraction of our blood and eventually tissues and organs with others. And of course there are possibilities that no one can now foresee. The important principle from the genetic standpoint is that following each environmental improvement there is a slow return to the old mutational equilibrium. We cannot maintain the present low death rate forever by simply maintaining the present environment; continuous improvements have to be made. Whether future health is better or worse depends on the relative rate of environmental improvement compared with mutation accumulation. Much of the long-range success depends on economic advance that makes possible a large expenditure in repairing one another's genetic weaknesses.

Perhaps most important of all for man's genetic future is the finding of substitutes for natural selection. Natural selection operates in an inefficient and often cruel way. What are needed are ways of painlessly and efficiently weeding out harmful mutant genes. There are several possibilities that offer hope for the future. Increasing knowledge of biochemistry has made it possible to detect persons who are asymptomatic, but who may pass on the gene for a severe disease. Ways may some day be found to identify persons who carry a large number of genetic defects, so that one abstention from reproduction may eliminate several harmful genes. Artificial insemination and, some day, perhaps, ova transplants may be used. With these possibilities, and with the advances that are certain to come in the future, man can go a long way in replacing natural selection with much more effective and much more humane alternatives. I have more confidence that scientists will be able to devise such procedures than that society will accept them willingly and use them wisely.

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THE POTENTIAL CONTRIBUTION OF LONGITUDINAL TWIN STUDIES

An Appraisal*

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Introduction

IN GENERAL DISCUSSIONS INVOLVING representatives of the varying disciplines of human biology, it is apparent that most authorities agree in considerable measure superficially, but there are certain basic fundamentals they do not agree upon. This leads to the proposition that more information is needed in the basic sciences in the disciplines connected with problems of growth and development.

In studying some of the many problems there is a need for cooperation of many different investigators and a strong plea for the interdisciplinary approach must be lodged at the outset. To give an example, in studying the genetic effect on growth and development, there is no sharp dividing line between, for instance, psychological and physical investigation. It is vital to record this view.

Clearly in the study of this complex subject we must accept the fundamental hypothesis that the overall gene "stream" of an individual runs through and under many influences which may be summarized as environmental, and, of course, hereditary. These two basic influences on growth and development with ultimate formation of a "type" of individual are irrevocably inseparable. What is wanted in the many branches of the fields of investigation under discussion is to know the weighting of the influences, and then how the results may become set or altered; and how the genetic stream may be affected by cultural, educational, physiological, and physical influences, which are quoted as clear-cut examples.

The human biologist eagerly seeks knowledge on the structural and behavioral patterns and their variations. It is a constant stimulation that in spite of the great amount of work carried out in the field in the past we still know surprisingly little about patterns of development, and especially correlations between them.

There are a great many facets of an individual, and his changing curve of development is indeed complex. D'Arcy Wentworth Thompson (1917) wrote: "A curve of growth to run all life long is only simple in the simplest of organisms, and is usually a very complex affair." What is confusing is that the differing characteristics are inter-related and influence each other. Some of these facets appear to change little in life—and it may be upon these that we rely to determine an individual's character, or "make-up," in the widest sense. Knowledge on such problems is fundamental for investigation in the basic sciences.

It is apparent that the final characteristics just discussed may be laid down in childhood and influenced sharply by environmental influences in this period. Mind-

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ful constantly of genetic influence, it is therefore important to study the child from these aspects on an inter-disciplinary and longitudinal basis.

It is perhaps important to say what is meant by longitudinal basis. Clearly it is easy, or easier, to obtain cross-sectional figures upon growth and development in any population. This consists of measuring for some factor a large number of individuals at the same time, at a certain age in childhood, or in adulthood. According to the worthiness or representation of the sample we gain information on the state of that measurement at certain points on a developmental curve.

With a changing organism, and certainly from the research point of view, it is more profitable and often necessary to study the organism as it changes to find out, for example, its speed of growth. If something is moving, you need to know at what speed it is moving. This can only be done by the longitudinal approach.

A child investigated more than once provides two measurements; the first measurement is subtracted from the second and the result is data vital to the researcher in the field—the incremental figure. It is not permissible, as one often sees in the literature, to deduce incremental figures from cross-sectional data. It is fully realized that the longitudinal approach to developmental problems is expensive and fraught with every kind of difficulty, but in the investigation of a changing organism it is difficult to see an alternative approach.

"Is maximum growth optimum growth," and such other stimulating questions cannot be answered unless you follow the growing organisms over a long period of time, and, indeed, there are some problems which cannot be investigated unless the organism is followed from birth to maturity. In fact, it is pertinent to note that environmental influences do not start to operate at birth but theoretically at the moment of conception. The fact that one can come from a good home or a bad home *in utero* is important and all too often neglected. Means of studying this prenatal environment are difficult but by no means impossible, as will be suggested.

A possible suitable method of study, based upon investigations of twins ideally from before birth, will be proposed.

It may be asked why it is necessary to center such a study on childhood. The crux is that as differentiations appear they presumably become fixed at some time in childhood. The varied influences can be seen acting, and their effect assessed. Clearly many problems, as has been mentioned, can only be solved by following children until they actually become adults, for in some children differentiations in childhood may be temporary and may not always persist to adulthood. The main aim, then, would be to study the inter-relation and identification of the many factors which lead to a differentiation of the character and "type" of the child or adult. "Type" is used here in the very widest sense. The diverse influences acting on the development of the child may be summarized from the investigation point of view under the headings psychological, physical, and physiological.

Mindful of these introductory remarks, it is obvious that investigators in the growth field and geneticists might turn to studies of identical twins. Such studies have been done before, and this is an idea, of course, which is by no means new.

Historical

Francis Galton founded the science that might be termed "Gemellology" in 1875 and 1883. First, his paper on "The History of Twins as a Criterion of the Relative Powers of Nature and Nurture," and then his book "Inquiries into Human Faculty and Its Development," showed that the proposed investigations were to throw light on the weight on "just scales of the effects of Nature and Nurture, and to ascertain their respective shares in framing the disposition and intellectual ability of men."

Thorndike in 1905, and Poll in 1914, published results of the measuration of twins, and in 1923 Apert and Siemens separately provided more comprehensive publications dealing with biological and pathological considerations. These scientists may be said to have been the pioneers. Dahlberg (1926) gave the first detailed work on the inheritance of physical characteristics which is a milestone in this history. Similar work was carried out by Stocks in 1930. It does not seem to be widely known that important publications were being produced from the Maxim Gorky Medical-Genetical Research Institute in Moscow up to 1936.

Professor S. G. Levit, its director, disappeared some short time after this, and little more has been heard from this important center. A large number of carefully documented twins were followed and investigations covered a wide range. Sobolera and Ignatier (1936) on the role of heredity and environment in variability of height and weight; Lichtenstein and Bassina (1936) on the mouth cavity in twins; and Lunia and Mirennova (1936) on the stability of the effect of training, serve as examples of the important work using twins as subjects which was carried out by members of this Institute. The production of appreciable differences in monozygous twins after the action of "exogenous" postnatal influences was shown by Komai and Fukuoka (1934). The classical work of Newman, Freeman and Holzinger was published in 1931 and described the investigations into identical twins who had been separated at birth or early in life and had been brought up in different environments. A general account of twins under study has been described by Gedda (1951). Penrose in 1937 reported a pair of monovular twins in which only one had congenital syphilis. This stimulated the very necessary interest in pre-natal influences upon identical twins, and these recognized pre-natal factors have been given in review form by Bass (1952). It was Price (1950) who pointed out our need to consider these biases of pre-natal onset which he maintains influence the development of twins. He divides them into natal factors, lateral inversion, and the effects of mutual circulation. These biases may affect both types of twins, but to a varying degree. Neel (1956) has suggested that "evidence on the magnitude of the biases must be obtained if we are to determine whether the twin method can be properly implemented as a tool for the appraisal of a nature-nurture interaction."

Despite the past excellent work done upon twins and briefly reviewed here, there is a need for a longtitudinal interdisciplinary study, in the widest sense, carried out over a number of years.

In summary, unusual opportunities are afforded in the study of monozygous and dizygous twins and their siblings on a longitudinal basis to elucidate the weightings of genetic and environmental influences. For a long time the dramatic concordance of the monozygous twin in psychological, physical, physiological, and pathological considerations has been an attractive and noticeable feature, but it should be brought to mind that it will be *discordant* features that will lead to greater knowledge concerning our problems.

International Cooperation

At this point it is necessary to digress and to describe some international growth studies which are at present in progress in Europe and Africa. Very briefly, the historical beginning of these growth studies started with an interdisciplinary longitudinal growth study in the widest sense in London approximately six years ago. This was not concerned with twins in any way. It was a study on so-called "healthy," randomly-selected children from an urban population, and the principle was to study them on a birth-to-maturity basis.

It was the desire of French colleagues that they start in Paris a similar growth study, the plan being to run on exactly parallel lines to the London study. It then

became apparent that other centers were interested in cooperating in this way and the writer foresaw the possibility of spending a life going around the capitals of Europe starting growth studies. This was alarming. The bringing of order, into what promised to be a possibly chaotic house, was effected by sponsorship of the International Children's Center in Paris. In short, there are now running five European longitudinal growth studies. They are all interdisciplinary. The principle behind them is that all have agreed to follow a very simple—and simple is emphasized—"base line" of investigations in all the disciplines (Falkner, 1957i). It is essential to note that no central "authority" is directing these growth studies. They all have very special interests and in some branches are doing very detailed work. That, in a way, is not the concern of the international group. What all have undertaken to do is to follow this agreed international base line.

Clearly, the base line must be improved, criticized and altered continually, especially on the psychological side, as the children are growing older. It is, therefore, necessary to meet regularly to do battle, criticize each other, compare data, plan work for the following year, and to standardize methods and techniques.

This international cooperative work is presented here, for its potential advantages are obvious—the production of comparative international data. There are two studies in Africa which are clearly on groups of very differently constituted samples of children, malnutrition being one of the big factors of difference. Their participation will lead to comparisons of great interest. These centers are in West Africa and East Africa, and the base line is used as far as possible. Already, although some of the growth studies are comparatively new, it is apparent that the African child, certainly in the first year of life, has a different pattern of mental and physical development compared to the European child. Allbrook (1956) has recently shown that there is a reduction in the adrenal cortical mass in the East African compared to the European. Such work stimulates one to speculate on the basis for such differing patterns of development and enhances the plea for more of such basic comparative data. The importance of studying the Negro comparatively in the United States is also clear.

Quite apart from the advantages of using truly comparative international data, the solution of such problems as the influence of racial factors upon human variability may be further investigated following such original observations as those of Muller (1954).

The Longitudinal Approach

To gain approval for such a proposed type of project is not easy. The reason is clear. Experience has shown that this type of study has not always been satisfactory from every point of view.

It is fully recognized that some problems can only be studied by following children from birth to maturity. The objections to this method are that it has been thought necessary to wait a great time before analyzing the data. Such growth studies have been attempted in the past and, with others, have collected large quantities of data which, excellent as they are, have been insufficiently analyzed because of difficulties to which all are fully sympathetic. There is a further danger in interdisciplinary long-term studies of this kind in that the various disciplines become bogged down with data which is sequestered and not coordinated.

Mindful of these disastrous pitfalls, and with these uppermost in thought, a solution is to follow children routinely on a "mixed longitudinal basis." The basic principle behind this is to recruit children in groups at all ages. This method enables investigation to be carried out on a whole age range of development by means of several overlapping longitudinal runs. Con-

veniently, these would be in five-year periods, and the important adolescent group would be included in the last two. The adult will be mentioned later. This method produces results much more quickly, and the investigators will clearly at the same time gain a much larger overall experience with the growing child in his entirety and in all the disciplines.

Although the work would be planned basically in runs of five years, it will be to everyone's advantage to follow some of the children for as long as possible, and to hope to follow the majority to maturity. It would be very desirable to recruit as many identical twins as possible before birth, and the expressed interest, for example, of obstetrical and radiological colleagues would ensure this. After recruitment of groups of monozygous and dizygous twins, the siblings ideally should be studied. An energetic attempt should also be made to find the greatest possible number of monozygous twins who had been separated in childhood. It is recognized that these are very rare.

In view of past experiences with growth studies in general the following is stated with considerable trepidation, but honesty requires that it be stated: It must be recognized that many basic problems of growth and behavior are unsolved. In any longitudinal multi-disciplinary project data is collected in quantity. In addition to clear-cut hypotheses to be tested—and these are essential—it is always probable that profitable lines of research and possible correlations, and so forth, will develop as the research does. It is best to clearly state this, and this concept is strongly claimed to justify *some* part of such a study's usefulness. The great pitfalls apparent when using this perhaps comforting hypothesis must be, and are, recognized.

A further aim is to provide information for other workers in the field. It is obvious that possible correlations would be very large. If the data is in a workable form, it is invaluable from time to time for specialized researchers who may require information from one part of the work. This has occurred successfully five times within the last three years in the cooperative European studies.

There is always the problem of keeping contact with a "longitudinal sample" and in large countries the geographical considerations of the moving members of the samples can be a source of worrying loss. It is, therefore, important to prophesy such a loss in order to minimize a final result of finishing with a sample too depleted to sustain reliable results.

One aspect of such growth studies in general is neglected: Their value as a teaching tool is not always appreciated. They can contribute much to post-graduate and graduate education during their actual routine and progressive existence while the educational value to the investigators themselves is large. In making a plea for this kind of work it is necessary to produce every possible advantage.

The great pitfalls, then, apparent when following the methodology of this type of research, are: (1) Over-collection and storage of large quantities of data. This may be largely overcome by the use of mechanically recorded data, and using modern statistical techniques and computation (Heumann, 1956). It is fully realized that by placing data on IBM cards, for instance, the problems of actual analysis of data are by no means solved. It does, however, place the data in a workable condition. (2) Lack of constant review of data. Such review should be stimulated by: (a) An Advisory Board, and (b) the availability of data for use of other research workers.

A word on "an Advisory Board": Entering the field of investigation into problems of growth and development is not unlike taking off across the high wire. Falling off is easy but staying on is not, and to undertake investigation into this sphere without the constant supervision and skilled help of a geneticist and biometrist is asking to fall very early in the precarious journey.

The advice and planning of a social science expert is also essential in order to be sure to investigate skillfully the all-important "socio-environmental" background of the subjects. Thus, the interdisciplinary approach must be carefully planned and the investigations themselves supervised by such a regularly meeting advisory body.

The Twin Study

Before carrying out any investigations, it is clearly essential to classify the twins studied and designate accurately the monozygous from the dizygous. Study of the placenta is important, and microscopic examination may be necessary but not conclusive. It is common that monozygous twins may exist *in utero* in separate fetal membrances for example (Von Vershner, 1939), and indeed may have separate placentas (Lassén, 1931). Other such diagnostic factors as concordance of sex, physical features, skin, hair and eye color, taste perception for phenylthiocarbamide, tongue curling, and fingerprints and palm prints are all of help in determining monozygosity. But at best their conclusiveness is never of complete certainty. It is of interest that authorities now make clear that fingerprints of identical twins are not necessarily identical (Federal Bureau of Investigation, 1953).

Happily the basic work of Race and Sanger (1950); Fisher (1951); Weiner (1935, 1940, 1952); Bryce, *et al.* (1951); and Walsh (1955) on the concordance of blood factors has made it possible to determine the truly monozygous pair with great accuracy. For theoretical considerations, use of the previously mentioned concordance factors together with determination of the ABO, MNS, and RH blood groups will ensure correct diagnosis.

Basic Hypotheses

There are three hypotheses to be tested which are vital and basic to interpretation of twin study data. In the past these influences may have been recognized as possibilities, but their effect has not been assessed. Hence, all work in this field is based upon assumptions which have not been and must be tested. These are: (1) that differing pre-natal and natal influences upon each twin of a monozygous pair cause discordant patterns of development. (For example, abnormal positioning *in utero* of one twin.) (2) That concordance in patterns of development of dizygous twins may be due to, or influenced by, a common circulation while *in utero*. Concordance held to be due to similar environment may be, in effect, due to this factor. (3) That certain definite maternal influences pre-natally produce discordance in monozygous twins. For example, one pair of monozygous twins had congenital syphilis and not the other. (Penrose, 1937)

To test these hypotheses, a group of prenatally recruited twins are needed and the cooperation of skilled obstetric colleagues required. After the thirty-second week of pregnancy positioning of each twin is rarely altered and careful observation at the birth should label each twin. Routine radiographic examinations are normally carried out after the thirty-second week and this further gives information as to the positioning. (Extra radiography for this study is not justified with the current consciousness of the effect of radiation on the fetus.) Regular plotting of the position of each fetal heart will be an added indicator of position, since the differing fetal heart rates commonly remain so. Labeling and accurate microscopic and macroscopic examinations of the placentas are necessary and practical, while an accurate maternal history during pregnancy is mandatory.

The subsequent groups of monozygous and dizygous twins form control groups.

Research on human twins has often had to be retrospective and obviously has involved twins who have both lived a certain time and usually a comparatively long time. The method of ante-natal study allows of the possibility of studying twins with the *prospects* of a long-term follow-

up; and perhaps more important of studying twins where one or both die before birth; and aborted twin pregnancies. Investigation of such aborted or still-born twins, coupled with histo-chemical and biochemical studies on healthy and diseased placentas in monozygous and dizygous pregnancies should reveal valuable information.

Further Investigations

In general, the lines of investigation of the proposed interdisciplinary study would proceed along the main lines already discussed and hypotheses other than the above basic three would be tested in the different disciplines of the research. It would be undesirable to carry out a great mass of highly detailed investigations on *all* the twins, for example. Sub-groups would be formed where suitable.

It may be profitable to discuss at this point some examples of problems from the various disciplines which should be investigated in such a study. Along the *physical line of approach*, Palmer (1934) has suggested that genetic determination of the *rate* of growth is likely to be independent of genes influencing *size* achieved. Further general work on this subject would clearly emerge. A most profitable feature would be to break down the growth in the twins to the unit involved: as an example, the whole concept of skeletal maturity is under discussion, for its accurate measurement is advantageous in many spheres. (Falkner, 1957ii). More information is needed on the genetic influence on the *pattern* of the individual variations in skeletal maturation before such improved assessment is possible. (Reynolds, 1943; Garn, 1956; Acheson, 1956). Patterns of development are always of interest to the growth investigator and these would, clearly, merge. A particular current interest is centered on the patterning of fat growth in the human, and the investigation of true genetic influence on obesity and the "normal" large variation of fat distribution in the child and adult would be profitable.

Physiologically certain problems present themselves for disentanglement. Two important examples are given: Are enzyme levels in the child genetically determined? And possibly more important, is the pattern of antibody formation in the human genetically determined? It is more correct to say in place of "genetically determined," is the weighting very heavy on the side of the genetic influence? Basic information on antibody formation is vital to us in the field of preventive medicine in the future—our synthesization of antibiotics may not for long outstrip the rate of sensitization of organisms.

Dobzhansky (1957) has pointed out to us that growth does not stop at the age of 20 years in the human but is represented by a trajectory which falls off at senescence. This is true, but it is continually fascinating in examining the incremental curves of size of many parts of the body to see how dramatically these incremental figures drop to zero at approximately the age of 20 years. Why does growth of size stop at this point and stay at the same point for often 40 years? Growth, to make a generalization, occurs by cell division rather than increase in cell size. (Neural tissue is a clear exception.) In some organs or tissues there are, then, two processes occurring during the active growing phase—cell division, and repair or replacement for regenerative processes. Clearly calories are needed for both; but a highly speculative suggestion is made that a constant supply and amount of a substance (say *M*, signifying mythical) is available which is quantitatively genetically determined, and which activates the division and regeneration process. When a certain size of that tissue mass is obtained, the regeneration now necessary for its constancy will use all the substance *M* available, and hence further calories above a basic amount will not result in any cell division and thus no in-

crease in size. Investigation at a basic level along this avenue might have a wide application.

In the area of *pathological processes*, it will be particularly helpful to establish the weighting of conditioning of disease by inheritance. Twin studies are a profitable field for such investigation. Warkany, *et al.* (1955) have described discordance in monozygous twins resulting in diabetes mellitus in one twin and obesity in the other. They point out the importance of this and similar observations for the study of the etiology of diabetes mellitus and of obesity.

Work on the inheritance of susceptibility to infection by tuberculosis was stimulated by Diehl (1933, 1936) and recently by workers in France. These are important indications of the part twin investigations can play in elucidating such important information of this type.

It must have been evident by now that this discussion has been centered very largely on fields of investigation other than the *psychological* one. It must be emphasized very strongly that this is not because of a reluctance to admit of its great importance, but it is simply due to an unwillingness to discuss something in which the writer has no special knowledge. With this reservation, however, some of his colleagues' observations and general ideas are put forward. Thompson (1957 has shown us that with modern mathematical, statistical and experimental psychological methods we are able to be far more objective today than we ever were before. On a very simple level, the psychological investigation methods as used in the international base line are summarized. This will show the basis of proposed work in this field for use in a twin study.

1. The interrelation of psychological influences with others affecting the behavior and development of the personality of the child is studied. In avoiding detailed description, the principles of investigation may be divided into (a) interview techniques. Here data obtained from interviewing the mother and close relatives of the child, and older child himself, is collected. (b) Standardized testing techniques for the assessment of the child's mental ability. These vary naturally according to the age of the child. It is pertinent to note that work has already been carried out by the international teams on attempting to assess present tests and devising new ones, particularly for the very young child and the infant. In respect to both of the above basic methods it should be pointed out that both are constantly subject to review and attempt at improvement. (c) Assessment of the temperament of the child by standard and experimental methods.

2. Assessment of the changing socio-environmental background of the child. This part of the investigation can be said to be vitally important to all sides of the research, but for the sake of convenience it is included under the psychological heading.

This sketchy account is merely the presentation of a non-expert in the field who realizes its paramount importance.

Constitution

Finally it is necessary to traverse the most slippery part of the high wire. In discussing the child and adults in growth and development studies, we are constantly coming across the concept of "types," "somatotypes," "body-types," "personality-types," and so on. It is clear that each of us has an individual subjective method of typing our fellow humans. This is not a new idea.

> "Let me have men about me that are fat, sleek-headed men and such as sleep of nights! Yon Cassius has a lean and hungry look, he thinks too much; such men are dangerous."
>
> . . . *Julius Caesar*
> Act 1, Scene 2.

Hippocrates (450 B.C.) described two types of people, apoplectic and phthisic, and the great clinicians in the past commonly gave us excellent constitutional descriptions of individuals with certain dis-

ease entities. Beneke (1878), the German pathologist, perhaps may be said to have founded the interest in constitutional disease. Two Frenchmen, Rostan in the middle of the nineteenth century and Sigaud at the beginning of the twentieth, started and continued the French "school" of constitutional classification of the human, and they divided man into "digestive," "muscular," "respiratory," and "cerebral" types. (Some individuals were not able to be fitted into these divisions and presumably were just unfortunate misfits.) There are still some French workers who adhere to this classification, and the school certainly stimulated work in the field. It was Kretschmer in 1921 who achieved considerable notice through his furtherance of this principle and he divided individuals into three groups: pyknic, athletic, and asthenic. Although Kretschmer was in fact working basically with mentally abnormal persons, and his notations have since been widely and very incorrectly used, his was the first real attempt to correlate character with body-type. His method was highly subjective, but he did at one time try to be more objective by physical measurements.

Since 1919, Viola, an Italian physician, has worked with the problem of constitution and its correlation with disease, and by physical measurements he devised an index of "morphological type." Here was a truly objective attempt, but he, too, placed the individual in three separate categories. It might repay us to study Viola's principles anew especially in relation to disease.

Up to this point the "constitutionalists" divided us into clear-cut categories. A newer development was that of factor analysis (examples: Burt, 1938; McCloy, C. H., 1940) which, reducing description to a very basic level, is a method of describing any physique conveniently as factors after statistical analysis of a series of correlated measurements. These measurements are anthropometric ones and what is actually measured is clearly important. (As far as is known no follower of this method takes into consideration the distribution of fat in the body.) Certainly this index moved us a step forward and did not place us in a pigeonhole.

Sheldon since 1940 (1940, 1942, 1949, 1954), has steadily put forward his important concept of constitutional factors. He, too, used a number of divisions of physical types, three—but with this vital difference —they became components and each individual type was assessed by means of the quantity present of each component. Sheldon's original work was highly objective and based on measurements carried out on standardized photographs of over 4000 young adult males. Since this time it has been realized that this method was too "static," and the present method now is to label the individual by division of subjects into age groups, the use of a height-to-weight ratio, and anthroscopy (or inspection of standardized photographs). This method, perhaps surprisingly to some, is satisfactorily objective (Tanner, 1954i.) I have carefully refrained from describing in words any of the physical types used over the centuries. Sheldon's nomenclature for the three basic components has caused some criticism, but I submit the actual names have really little importance. As a basis for research into the difficult problems of biological constitution it is clear a great amount of work has to be done, and it is timely to state that Sheldon himself has never stopped pointing out that his work and the work of others in the field (examples: Dupertuis and Michael, 1953; Tanner, 1954ii) is *provocative of new research*. The relationship of physique to temperament, that most fascinating of problems in this field, is the most controversial part of Sheldon's work, and it is here lies the stimulation for the beginning of a great amount of needed research. Do we not, all of us, have our individual methods of "rating" temperament as well as physique? Is there a true relationship between the two? Can temperament be altered? Is physique largely a static phe-

nomenon? Clearly not—but to what degree not? An ex-chief and friend, who was very much *not* of muscular athletic build (heavily endowed with "mesomorphy") and was very round, once asked me: "We should all like to be mesomorphs — how can I change; could I have done so whilst a baby?"

It is clear to me—and I am impressed by the number of colleagues who agree with me—that babies and children can be individually "typed" using the word very broadly. With the babies this is highly subjective. What is wanted is information on the type, not necessarily a static type reached at "maturity," but its continual trend or pattern of development. The work of animal physiologists (Hammond, 1954, 1955), stimulates us to investigate the changes of body build in the human basically genetically determined, for they have shown that differing nutritional status may produce great changes in configuration and actual body composition.

In the realm of environment, we are back into the concepts of the founders of constitutional medicine. I quote an example: Colleagues (Dowling *et al.*, 1956) are investigating the disease of infantile eczema (Prurigo Besnier) in a group of children. It is considered probable that this condition is a good example of "psychosomatic disease." It is becoming apparent to us that these children of all ages have a very large component of muscularity in their build. If this is proved and accepted at a scientific level, it is only one small step forward. The next and vital question is, what was, and is, the weighting of genetic and environmental factors which produced or altered the behavior, physique, and physiological state of a child so that he was more susceptible to this condition than if he were the child next door with a different make-up?

Newer objective provocative work on these fundamentals is being produced with the adult, examples of which are Gertler *et al.* (1951) on coronary occlusion, and Sutter and Tabah (1953) in France on the relation of consanguinity to the general structure of mortality.

In assessing the weighting of the genetic influence, it appears that a valuable contribution to this whole difficult field might be made by a long-term study of the human twin. It cannot be emphasized enough that great harm has been done in the past by some unscientific approaches to these problems and any future work from whatever angle must be made from an interdisciplinary standpoint and with rigid scientific standards. A collective approach to these problems should yield valuable results with simultaneous assessment of shape and constitution using psychological, anthropometric, biochemical, photogrammetric, radiological measurement, and volumetric estimations. But is an unraveling of the place of the genetic, physiological, and psychological biases as influences on human constitution likely to contribute to biological knowledge of the human? Surely, for ". . . morbidity and mortality constitute the long range criteria of the importance of differences in human physique" (Brozek, 1956).

Some varying components of temperament, behavior and body composition are influenced greatly by the human variables which we have discussed. All these variable aspects present a problem for further rethinking and research. Valid information on this subject gained by impeccable scientific attempt is needed and may be evaluated in degrees of future human health and happiness. It is a challenge of high endeavor to human biologists—a challenge full, I am sure, of heartbreaks but it must be taken up for the rewards will be very great.

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GENETIC ELEMENTS IN SCHIZOPHRENIA

A Review of the Literature and Resumé of Unsolved Problems

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IT HAS OFTEN BEEN EMPHASIZED, most recently by Planansky (37), Schulz (48) and others, that the evaluation by a psychiatrist of the genetic theory of schizophrenia is neither a matter of personal conviction nor a measure of loyalty to a certain school of training and thought. As in every other case of unclear etiology, the decision to accept or reject the genetic hypothesis should depend on the type of evidence accumulated and on the soundness of the conclusions drawn from these data.

The significant part played by non-genetic influences in the pathoplastic and psychodynamic aspects of schizophrenia has been discussed in previous reviews. Since that part has never been minimized by a geneticist of the modern variety, this review will be limited to studies concerned with the genetic elements in the etiology of schizophrenia. Apart from seeking an answer to the question of whether or not there is sufficient evidence for a genetic determinant or predisposing factor in this type of psychosis, an attempt will be made to review the historical development of genetic investigations in this area, how much is known about the heredity factor at this point, and how many problems are still unsolved.

Throughout this review, it may be helpful to keep in mind that from a genetic viewpoint a deviant behavior pattern is not considered as the result of a simple genotype-phenotype relationship, reducible to an aggregate of well-defined and easily differentiated interacting influences. A psychotic behavior pattern is not simply regarded as the concomitant of a fixed congenital aberration any more than it is thought of as a self-limited error in homeostasis, or an unfortunate episode in adjustment. Genetically, a psychosis is viewed as a complex and continuous process in the biological history of the individual.

This general principle has been expressed by Planansky as follows:

"Simply ascertaining the presence or absence of psychosis in members of a family for the purposes of statistical analysis is apt to bring forth only partial information on outwardly observable characteristics of lives whose biological uniqueness remains unknown. The study of heredity and environment in human lives is facilitated by a dynamic concept of constitution, based on genic endowment. Continuous adaptive changes take place as new, genetically determined functions in their appropriate time enter into the individual's physiology, in order to fulfill life according to the image of the species in the prevailing environment. The cumulative effect of adaptive responses to environment in effect becomes incorporated into constitutional potentialities."

Methods of Genetic Investigation

The implications of this broad biological principle make it desirable to begin with a review of the methodological and historical aspects of genetic investigations in psychiatry. For obvious reasons, the technical and conceptual difficulties inherent

in population studies are particularly pronounced in this field.

1. The simplest and by far the oldest procedure is the pedigree or family history method. Even in the pre-Mendelian period —that is, long before the disease entity called dementia praecox had been established (1895)—many case reports were placed on record, which aimed at confirming the commonplace notion that psychoses tend "to run in families." Unfortunately, in a mental disorder which is as common and symptomatologically diversified as schizophrenia, the statistical value of such studies, quite popular until the early 1900s, is extremely limited. These limitations are not so much due to a lack of Mendelian orientation, which began to assert itself in the early 20th century, as they are due to the fact that older case reports were usually restricted to "interesting" family cases, loaded with what was ascribed to heredity, in order to prove the point. Obviously, however, the observation of a large number of schizophrenics in a given family, while suggestive of a gene-specific mechanism, does not rule out such other causes, as an unknown type of infection, psychic contagion, some special dietary or climatic deficiency, unusual stress factors, or the like.

2. The need of studying the heredity problems of schizophrenia in statistically representative and clinically homogeneous samples was recognized first by Rüdin (40), whose classical monograph "Zur Vererbung und Neuentstehung der Dementia Praecox," was published in 1916. In the procedure developed by Rüdin and his school, especially by Weinberg (60), Brugger (5), Kattentidt (23), Luxenburger (29) and Schulz (45), the statistically corrected expectancy (or prevalence) of schizophrenia in the general population was compared with that observed in different groups of relatives of schizophrenics.

Using this method, named the contingency method of statistical prediction, Rüdin conducted the first study of a sample of sibs and half-sibs of schizophrenics, that was later re-examined by Schulz as well as by Luxenburger (1930). Hoffman (13), Gengnagel (11), and Oppler (33) studied small groups of children of schizophrenics, while other investigators [Schulz (44), Walker (59), Konstantinu (25)] obtained comparable data on nephews and nieces, great nephews and great nieces, and first cousins. Kallmann's (16) first survey was focused on the expectancy of schizophrenia in a large group of descendants of schizophrenics and their sibs. All of these studies were completed by the mid-1930s. With respect to general population samples, that is, the ascertainment of schizophrenia rates for the general population, improved methods were subsequently devised by English and Scandinavian workers, notably by Essen-Möller (8), Fremming (9), Larsson and Sjögren (27), Slater (52), and Strömgren (57). Every one of these studies showed a significant difference between familial concentration and general prevalence of schizophrenia, with an increase in crude or statistically corrected expectancy rates observed in the different categories of relatives investigated, as they approach the schizophrenic family member in degree of genetic similarity. Considering the quantity as well as the quality of these studies, only some of which have been mentioned, and in view of their unanimity in this respect, it is highly improbable that further investigations will materially alter the pattern of distribution as indicated by this type of study.

The following is a range of the expectancy rates found by various observers in the different categories of relationship to schizophrenic probands:

General population	0.85%
Half siblings	7-8%
Full siblings	5-15%
with most investigators agreeing that the incidence is over 10%	
Parents	5-10%
Children (of one index case)	8-16%
Children (of two index cases)	53-68%

The fact that the given individual rates vary from observer to observer can be easily

explained when the difficulties encountered in this type of investigation are understood. Since each individual must be considered non-schizophrenic unless tangible evidence of the disease can be obtained, the rates found are minimum expectancy rates. That is, in investigating a series of siblings, those who are known to have been shiftless but remain unavailable for the study cannot be classified as schizophrenic, although their absence does not preclude such a diagnosis. In a study focusing primarily on the children of schizophrenics, the index cases must be parents, and thus be selected in such a way that their children will be old enough to have passed through the period of risk (15-45 years of age). If an attempt is then made to investigate the sibs and parents of the index cases in addition, it is to be expected that, due to migration or death, many potential schizophrenics will be missed in the older groups. In such a study, therefore, while an accurate expectancy figure may be obtained in the descendants, only a minimal rate is ascertainable for the sibs and parents of the index cases. On the other hand, in focusing on the sibs of schizophrenics, the investigator is forced to select probands who are young enough to have many siblings who are still alive and available for a concentrated study. This procedure necessarily limits the number of children who have lived through the age of risk. Another uncertainty affecting the results of different investigators is the fact that diagnostic criteria vary from country to country and from decade to decade. Investigators who have to use hospital records extending over two or more generations are apt to produce results which differ from those obtained with a direct diagnostic interview technique. It is remarkable, therefore, that in spite of the different investigative techniques used and the inherent tendency of the structure of the studies to reduce observable expectancy figures, there is unanimous accord in the finding that the various categories of blood relatives of schizophrenics show significantly higher incidence rates than does the general population.

3. The third method of genetic investigation is the comparative study of twins. Twins offer an unusual opportunity for studying the interactional aspects of genetic and non-genetic factors in the production of abnormal behavior patterns. The variables are the genotypic identity or non-identity of the individuals, and the varying degrees of similarity in their life conditions. In earliest studies, the histories of interesting twin pairs were described as a matter of curiosity. More recent data were obtained by serial studies, in which each twin was compared with his partner. Early but fairly extensive studies were especially those by Galton (10) in 1883, who was followed by Siemens (49), Von Verschuer (58), and Lange (26) in Europe, and by Gesell (12), Rosanoff (41) and others as early as 1911 in the United States. With progress in the accuracy of zygosity determination, and improvement in the system of psychiatric classification, psychiatric data of more than historical interest were published by Luxenburger (30) in 1930, and by Rosanoff (43) in 1934. These studies were limited in sample size, and no longitudinal follow-up was attempted. Although concordance or discordance of the twins as to schizophrenia was established only at the time of the first investigation, significantly different concordance rates were obtained for the monozygotic and dizygotic groups. It was Kallmann, in 1836, who planned the first large-scale unselected sample, followed by Essen-Möller (7) in 1941, and Slater (53) in 1951 with series of significant size. In 1946, Kallmann (17) reported on the most extensive twin series to date, including over 1100 twin pairs, over 950 of whom were schizophrenic. Combining the twin study method with a sib and family investigation, he obtained a series of comparative expectancy rates for schizophrenics with respect to all the varying degrees of genetic similarity to a schizophrenic proband. His cases had been followed for longitudinal

study for a minimum of five years.

The range of schizophrenia rates found in twin studies is as follows:

Concordance in dizygotic twins (one twin being the index case)	3.3-16.7%
Concordance in monozygotic twins (one twin being the index case)	66.6-86.2%

It is again worthy of emphasis that all investigators observed a significant increase in concordance from two-egg to one-egg twins. Of equal importance was the finding that the expectancy of the dizygotic twin of a schizophrenic proband proved to be approximately the same as that of other sibs (10-15 per cent), regardless of the fact that twins usually share the same environment at a comparable age.

Mode of Inheritance

None of the investigators who used either the contingency method or the twin study method was able to explain the increased incidence in the various categories of relatives of schizophrenics without assuming the existence of some genetic factor. In many studies attention was paid to economic status, to the frequency of sharing the milieu of an affected person, and to other facets of the individual's life conditions. Twin studies took into account such factors as order of birth, prematurity and birth weight, breast feeding, rate of infant development, intelligence, and handedness. None of these factors was found to be significantly associated with the occurrence of the psychotic process.

With the data requiring the assumption of a predispositional factor, the investigators felt obliged to explain its mode of transmission. Early observers were handicapped by the fact that the concepts of penetrance, expressivity, and modifying genes had not yet been formulated. In other words, they attempted to explain empirical findings according to simple Mendelian laws alone. Thus, Rüdin, in 1916, suggested two recessive genes to be responsible. This theory was based on his finding a rate of less than 5 per cent for schizophrenia among the sibs of his index cases in his first analysis. However, the same material when later reviewed by Schulz and Luxenburger yielded a considerably higher sib rate. A few years later, Hoffmann proposed either a two- or a three-factor type of recessive inheritance. About the same time, Kahn (15) expressed the belief in his monograph on schizophrenia and schizoid personality that the genetic mechanism seemed to be the same for both conditions. He thought of a dominant mode of inheritance, because of an apparently equal distribution of schizoid personality types among sibs and children. Later, in the 1930s, Kallmann assumed that a single unit factor was responsible for all clinical forms of schizophrenia, because of the observation of similar and dissimilar clinical forms of the disease in the same family. He believed this factor to be autosomal-recessive and subject to modification by other genes conferring a greater or lesser degree of resistance upon the individual. Especially in Germany during the 1930s a simple dominant mode of inheritance was favored and became the basis for eugenic sterilization laws. Since that time, it has been recognized that a recessive transmission is more likely. There are, however, a few old-timers such as Lenz (28), Koller (24), Slater (54) and Böök (3) who still support the theory of dominance.

Corroborative evidence for a recessive hypothesis would require a greater frequency of the disease in the sibs of an index case than in his children—if random mating is assumed, an increased frequency among the children of consanguineous parents, and a high frequency of the disease in collateral lines. While comparative studies of sibs and children have been inconclusive in this respect, there appears to be a positive correlation between incidence of schizophrenia and consanguinity of parents. Weinberg and Lobstein (62), in a study of the Jewish population of Amsterdam, found a significantly higher percentage of schizophrenia in the siblings of index

cases whose parents were cousins, than among those whose parents were not related. This difference was observed although there were no cases of schizophrenia in any of the 27 parental cousin couples. In 211 twin index pairs without schizophrenia in their known ancestry, Kallmann found that 5.7 per cent originated from consanguineous parental matings. In some Scandinavian studies an increase in cousin marriages in the parents of schizophrenics was also reported. Collateral line investigations consistently yielded an expectancy rate in excess of that of the general population.

Those investigators holding to the dominant hypothesis base their belief on the reports of an equal or greater expectancy if the children of index cases are compared with their sibs, and on complex statistical comparisons of empiric figures. Since the rates found are known to be minimum rates for some categories of relationship and are subject to variability because of methodological difficulties, one wonders if conclusions based on formulae which treat these figures as absolutes are justified. It may also be noted that in the statistical treatment of such expectancy rates, random mating is assumed. In the light of modern psychiatric theories regarding mate selection, this assumption seems to be open to question.

Moreover, proponents of either mode of inheritance are forced to utilize auxiliary hypotheses. Kallmann believes in a single recessive factor as the main gene whose expression is modified by the action of other genes. According to Penrose, this is a multifactor type of inheritance, and in the opinion of Schulz, too, most people are multiple carriers, but there is one dominant gene without which schizophrenia cannot appear; others postulate a dominant gene with markedly reduced penetrance in the heterozygous state. Upon close scrutiny, however, the various theories and their auxiliary hypotheses have a good deal in common in spite of their apparent divergence. The need to extrapolate from empiric data, related to a prolonged and not yet clearly understood series of interactions, precludes the formulation of a precise theory. The diversity of the theories advanced would seem to indicate that until the pathophysiologic nature of the inherited vulnerability factor is identified, theories as to the exact mode of its inheritance will remain inconclusive. For assistance in this work, geneticists look hopefully to the biochemist.

Other unsolved genetic problems of schizophrenia have to do with the homogeneity and specificity of the schizophrenic genotype. Homogeneity refers to the question of whether schizophrenia is one entity derived from one genotype, or merely a phenotypic syndrome expressing various genetic combinations. With regard to specificity, the question arises, on the one hand, whether the genes predisposing to schizophrenia may not also predispose to other pathological behavior patterns, or, on the other, whether the genes are so specific that only Kraepelinian sub-forms of the disease are thus determined. The data available with respect to these questions are conflicting, and absolute answers have not yet been found.

It should be noted, however, that while many aspects of the genetics of schizophrenia remain as yet unclear, the results of genetic studies have served as a valuable point of departure for investigations in the fields of biochemistry and clinical psychiatry. An open mind towards the genetic theory of schizophrenia has led to interesting formulations concerning its essential psychodynamics. Most notable in this field is the work of Dr. Sandor Rado (38) and his school, who deserve credit for the attempt to explore the basic psychological organization of the genetically defined "schizotype."

Summary and Conclusions

1. The historical development of investigative procedures used in psychiatric genetic

studies has been reviewed. The various workers and their contributions to the genetic study of schizophrenia have been noted.

2. All the investigators have found increased expectancy rates for the relatives of schizophrenics as compared with the general population.

3. The effect of genetic similarity to a schizophrenic proband has been most clearly demonstrated by twin studies, comparing the concordance rates of one-egg and two-egg pairs.

4. While all available studies indicate a genetic factor in schizophrenia, efforts to explain the mode of transmission of this factor await the final clarification afforded by biochemical identification of what it is that is transmitted.

5. Although there is much that remains unsolved, the genetic theory has served as a valuable point of departure for investigations in allied fields. Its merits should be judged not by the amount that is still unknown, but by the multitude and quality of the data gathered by many investigators and by their usefulness in stimulating further penetrating and promising research.

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HEREDITY COUNSELING IN JAPAN*

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Recent Trends in Family Planning

JAPAN AND THE JAPANESE PEOPLE have changed in many ways since the last war. Public opinion concerning the significance of the growth of population in this country is one of many such changes. Before and during the war many people thought that such population growth was desirable as it provided more "human resources" for the nation. But today few informed persons take such a view; they are rather of the opinion that such growth is a menace to the welfare of the nation, and that effective measures to cope with the situation should be taken without delay.

The Eugenic Protection Law, first proclaimed in July 1948 and later amended several times, was designed mainly as one of such measures. Simultaneously a semi-official project for nationwide propaganda for family planning was planned and put into practice. The movement was reenforced by activities of private associations like the Japan Society for Propagation of Family Planning and has achieved great success, at least insofar as the people have become more conscious of fertility control. As a matter of fact the population trend of the country has changed abruptly in a short period. The practice of fertility control has become much more widespread than before. Still more striking, induced abortions have greatly increased. Government statistics show more than a million cases a year of induced abortions in recent years. If many more unreported cases are included, the actual number may well be double.[1]

The Eugenic Protection Law legalizes sterilization of either husband or wife or induced abortion if (1) the person in question or the spouse has a hereditary psychopathic trait, constitutional disease or malformation; (2) any relative within the fourth order (*i.e.*, cousin, great uncle, or aunt) of the person or spouse has hereditary psychosis, feeblemindedness, or a psychopathic trait. To offer effective eugenic protection to as many people as possible, Eugenic Protection Consultation Offices were established by law, one in each prefecture or city all over the country, and there are now about 800 of them. These offices provide anybody with information and advice on matters concerned with marriage. They also disseminate the knowledge necessary for eugenic protection and provide people with information about appropriate methods for pregnancy control. For the year 1955, a total of 151,755 consultations were offered in the Eugenic Protection Offices of the entire country (excluding those in Aomori Prefecture). These statistics are supplied by the Public Health Bureau of the Ministry of Welfare. The consultations may be broken down as follows: contraception, 105,589; induced abortion, 24,210; eugenic marriage, 7,354; unclassified, 14,602. It can be seen that eugenic marriage consultations constitute only a small fraction—less than 5 per cent—of all consultations. However, heredity counseling was probably offered not only to persons planning marriage but to people already married who felt the necessity for

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[1]See Induced Abortion in Japan by Thomas K. Burch, *Eugenics Quarterly*, Vol. II, No.3, 140-152.

induced abortion or contraception for some genetic reason. Statistics of the Japan Society of Propagation of Family Planning show that, of all 1,170,143 induced abortions in 1955, 1,492 were for hereditary reasons and 303 because of leprosy.

No details about the counseling in these eugenic protection consultation offices are known to the writer. It is likely, however, that information and advice are offered in accordance with the Eugenic Protection Law in which 6 mental diseases and derangements, 22 physical diseases, and 2 malformations are listed as undesirable hereditary traits for which sterilization or induced abortion is legalized. There may also be other eugenic problems on which consultant doctors formulate solutions and give advice even though their genetic knowledge of each problem may not be quite adequate.

Besides this "official" heredity counseling there is much unofficial counseling by individual geneticists who allocate special office hours for this purpose. Usually they give interviews to anybody who might come for counseling. They also answer questions on eugenic matters by mail. As one of such geneticists, the writer has had many chances to hold an interview with a stranger or a group of strangers who came with or without an introduction for eugenic information.

The Traditional Marriage System and Its Bearing on Heredity Counseling

According to the traditional marriage system in Japan, marriages are contracted primarily for the sake of the families instead of the individuals in question. Recently things have changed a great deal, especially since the war. The New Constitution demands that marriages are to be arranged entirely at the free choice of the couple and purely for their own benefit. Thus many modern marriages are actually contracted in accordance with this new principle. However, quite a few marriages —perhaps the majority—especially of the country people, are still arranged in accordance with the traditional system or by a compromise between the old and new systems. The elders of the families with young members of marrying age are anxious to find a suitable mate for them and take great pains toward this end. They frequently ask their neighbors and personal friends to introduce such a person to them. When a prospective mate is suggested, the elders gather all kinds of information about the person's ability, health, personality, reputation, etc., as well as about the personality and social standing of the parents and family members. Naturally the genetic background of the family is inquired after. Available information about the ailments of the family members and relatives are obtained from various sources. Not infrequently the elders call on geneticists or physicians for consultation and incorporate their advice into the evaluation of the candidate in question. Thus, rather strangely, marriage counseling in Japan is more commonly sought by people who stick to tradition than by those who are more progressive in their matrimonial attitude. Incidentally, it is certain that this traditional marriage system is responsible in some measure for the much higher rate of consanguinity among marriages in Japan than in European countries.

Examples of Heredity Counseling

1. *Consanguinity.* Consanguinity is the most frequent question all marriage consultants are asked about. Although each case differs in details, the general tenor of the writer's advice on the question is like this: As a general rule such marriages should be avoided as far as possible. This is especially true if the family on either side has someone with a hereditary disease or abnormality, the more so if the types of ailments on both sides coincide. In a consanguineous marriage a recessive gene for abnormality may become homozygous and produce patients. The rarer such a

gene in the population, the higher is the ratio of patients who are the progeny of consanguineous matings. Even when the trait is dominant, consanguineous matings may produce more patients with severer types of disease, apparently because such matings increase homozygosity of genes and decrease the role of so-called genetic homeostasis.

The following is an example of counseling offered by the writer on the subject of consanguineous marriages.

Lady A, member of a distinguished family, wanted to obtain as her eldest son's bride a daughter of her sister who had married into another distinguished family, B. The question of the proposed marriage was brought to the writer by a member of the B family for counseling. After inquiring about the pedigrees of both families, it was ascertained that one of Lady A's three sons was a deaf-mute, and also that Lady B.'s father-in-law was schizophrenic. Lady A attributed the deaf-mutism of the son to a babyhood accident when the nurse dropped him. It seemed rather doubtful, however, that this was the cause of the boy's deafness; rather the trait was suspected to be congenital. On purely genetic grounds the writer was inclined to disapprove arranging this consanguineous marriage. Apparently after some discussion and controversy among the members of the B family, they decided to decline Lady A's request. The prospective bride's reluctance to accept marriage seemed to be primarily responsible for this decision. She had previously visited a deaf-mute school and was informed that a surprisingly high percentage of the children in that school were the progeny of consanguineous marriages.

2. *Deaf-mutism.* This condition is one of the commonest hereditary defects for which marriage counseling is sought. The case of the noble family of Lady A is one such example.

Mr. T. Mori, a graduate of Kyoto University majoring in botany who had taught several years in a deaf-mute school in Kyoto, became interested in the genetics of deaf-mutism. He possesses a great deal of information about matings among deaf-mutes. According to Mr. Mori, the majority of deaf-mutes have a keen interest in marriage. This is particularly true of female deaf-mutes. Their parents want to take the first chance of marriage, presumably because they wish to turn over their handicapped children to a husband's care. The matings of deaf-mutes are frequently arranged by teachers of the school they attended. Some of the teachers whom Mr. Mori knows are proud of having arranged several of their students' matches. In many cases the union is between deaf-mutes, but it may be with a healthy mate. This is especially true when the deaf-mute bridegroom is a son of a well-to-do family.

Case A. The teacher of a local middle school had a normal son and two deaf-mute daughters, apparently of the congenital type. The elder daughter married a man who was also a deaf-mute but of non-congenital nature. The couple have children who are all normal. The younger daughter chose as her husband a classmate who was the offspring of a consanguineous marriage and who had a deaf-mute sister. Before the marriage the father of the daughters came for counseling to Mr. Mori and was warned against a possible unhappy outcome of the marriage. The young couple did marry, neglecting this warning, and have two children who are both deaf-mutes.

Case B. A tailor's son at the age of eleven started gradually losing his hearing, and he entered the deaf-mute school two years later. He had become stone-deaf when he graduated from the school after getting sufficient training to be a tailor. He chose as his fiancée a deaf-mute girl, apparently of the congenital type who was a skillful seamstress and who had at least one deaf-mute sib. Mr. Mori did not disapprove this match because the couple represented dif-

ferent types of deaf-mutism. The couple bore a normal child.

3. *Harelip and Strabismus.* Harelip is another common trait about which genetic counseling is frequently sought. It is often difficult to offer any clear-cut genetic diagnosis in each case, because certain cases of harelip apparently lack any genetic background. The majority seem to be due to a dominant gene. However, its penetrance is often imperfect, and a physically normal person may carry this gene and transmit it to the progeny in the same way as would the person afflicted with harelip.

We usually suggest that, if a relative of a person who is to marry has the deformity while the person himself is free from it, he should take a chance and marry. But if the person himself has the deformity, his relatives should be thoroughly investigated to see if any of them have the same condition. If a relative is afflicted, there is a greater possibility that the trait is of genetic origin. Then the risk would be rather high that an afflicted child would be born with the same deformity.

Cleft palate may be associated with harelip. Also cleft uvula has been suspected to be caused by the same gene as harelip. Therefore, it is safe to count these deformities in the same category as harelip.

Strabismus (squint), another common constitutional defect, is genetically similar to harelip in many respects: (1) The majority of cases seem to be of genetic origin and probably due to dominant gene; (2) The penetrance of the gene is often imperfect, and there is a rather wide range of variation in the expression of the trait; (3) There are apparently cases of non-genetic origin which are difficult to distinguish from those of genetic origin; (4) The deformity may be "cured" by an operation. Strabismus is somewhat commoner than harelip and obviously a less severe defect.

4. *Manic-depressive psychosis.* In heredity counseling on mental diseases the following case was encountered recently by the writer. A boy of marrying age had a sister who suffered from periodic attacks diagnosed by a psychiatrist as the manic-depressive type. His two aunts on his mother's side had had attacks of involutional depression. A friend of the family introduced a girl to him as a possible fiancée. Both the boy and his mother liked the girl. However, after investigating the pedigree of the girl the mother found that the girl's great aunt had suffered from mental disease after delivering a child. The mother brought the case to the writer for counseling.

The case was perplexing because there seemed to be mental disease on both sides of the families and the genes might coincide. The morbidity risk was obviously higher on the boy's side. However, neither he nor his mother (the father was deceased) had the slightest intention of rejecting love or matrimony. On the other hand the suspected case of mental disease on the girl's side was rather distant, and all other members of her large family were apparently mentally sound. So the arrangement of this marriage was not positively disapproved.

5. *Hemophilia.* A case concerning hemophilia was encountered by the writer recently in which no difficulty was found in answering questions from an academic standpoint but some difficulty occurred from the human relations viewpoint. One afternoon some months ago a middle-aged country woman came to the writer's office in the National Institute of Genetics and told the details of her family trouble. She was the widow of a man who had been employed in a neighboring factory and who had had a congenital ailment diagnosed as hemophilia. He suffered from swollen knees which had made it difficult for him to walk without a cane. He had died a few years previously from heart failure at the age of 51. His widow had two daughters of marrying age who knew that hemophilia was a serious hereditary disease and

were very worried about their matrimonial prospects. The daughters even condemned their mother sometimes for having married a man with such a dreadful hereditary disease. The mother wanted to make sure whether hemophilia was really a fatal hereditary disease and to ascertain the outcome of her daughters' marriages. It seemed certain the father's ailment had been hemophilia. Scattered cases of this disease are met with by local dentists in Japan. This man's hemophilia, however, was undoubtedly of a mild type since he lived to the age of 51 and had children. If the diagnosis were correct, the daughters should carry the gene and their sons, if they should bear any, would have a 50 per cent risk of being hemophilic. This information should be made available to the daughters.

A week later the same woman came in the office, accompanied this time by one of the daughters. The same story was repeated to them. We did our best to impress them with the fact that hemophilia is not the only dreadful hereditary disease and to suggest to them how to face the matter wisely and humanely.

6. *Leprosy.* Leprosy of course is a bacterial disease unlike any hereditary disease. However, families may occasionally be found in which more than one member is afflicted with this disease. Since the disease is a rare one, such a case might give people the wrong impression as if leprosy were a hereditary disease. Here and there in Japan one encounters a family which is rumored to carry a hereditary leprosic trait. Although such rumor is without any foundation, yet it is nearly fatal to the family as regards the matrimonial prospects of its young members.

The writer was once visited by a wife of a farmer living in a neighboring village of Misima, who told me that her son was going to marry a daughter in a family living in a distant village. The girl seemed an acceptable fiancée for the woman's son. After inquiries into the ancestry of the girl, the woman found out that the girl's great-grandfather's brother had deserted his home after contracting a disease apt to be leprosy. The woman and her husband were greatly perplexed by this information.

We encouraged the woman to disregard such a rumor for a number of reasons. The suspected case of leprosy was too far back in the feudal period when diagnoses of diseases were anything but reliable. The old man was not the girl's direct ancestor, and leprosy is not a hereditary disease. Even if there is variation among people as to susceptibility to this disease and this difference has a genetic basis — which has never been shown—the germ of leprosy is now so rare in countries like Japan that chances are negligible for ordinary people to come in contact with the germ sufficiently to become infected.

BOOK REVIEWS

THE EFFECT OF EXPOSURE TO THE ATOMIC BOMBS ON PREGNANCY TERMINATION IN HIROSHIMA AND NAGASAKI: J. V. Neel and W. J. Schull, Publication No. 461, National Academy of Sciences—National Research Council, Washington, 1956, 241 pp., $2.00.

The dropping of the atomic bombs on Japan can probably be excused as a necessary act of war. The same deed carried out as an experiment in radiation biology could not have been excused, however useful the findings. Just as inexcusable would have been a refusal to utilize the bombings, *fait accompli*, as a biological experiment. American officials and scientists quickly recognized their obligations in this respect, and the subsequent work of the Atomic Bomb Casualty Commission proves their dedication to this duty. The time and effort that have been expended in Hiroshima and Nagasaki to reap the maximum benefit in medical knowledge is impressively demonstrated in this book by the director of the Commission's genetics program and his associate. The magnitude of the survey here reported is matched by the thoroughness and sophistication of the analysis, and the result is a fitting monument to those killed or maimed by the first dawn of the atomic age.

The first six chapters are introductory, describing the setting for the study, its organization and difficulties, and the statistical tools applied. The next seven chapters present the data and their analysis, subject by subject: sex ratio of births, congenital malformations, stillbirths and infant deaths, birthweight and measurements at nine months, and infant autopsy findings. These chapters will have permanent value mainly as the record of a first-class infant health survey. Despite the authors' best efforts, their contribution to radiation medicine is entirely a negative one. Most of the significant statistical observations proved inconsistent from one part of the study to another, or were in a direction that defied genetic explanation. In the early years an impressive distortion of the sex ratio was interpreted as a genetic effect of the bombs, but extension of the data and more rigorous analysis failed to support that interpretation. Differences in body measurements between babies of exposed and unexposed parents were in the direction suggesting radiation damage, but they did not show the required dependence on degree of parental exposure.

The next-to-last chapter summarizes the analysis and reviews comparable observations of other workers in human and animal genetics. In the last chapter the authors stress the fact that any practical deductions from these data would depend on further facts that are as yet unknown, such as the natural mutation rate in man. They question the wisdom of calculations like those of Muller that are based on the assumptions that each deleterious mutation must cause one complete genetic death and that mutations are practically all deleterious. At present, they say both large and small estimates of the radiation hazard are consistent with our information, and this is only one of several dysgenic influences that human geneticists will have to evaluate.

This book will probably disappoint those who anticipated grave genetic consequences of the bombs. Even the less expectant reader may be dissatisfied to find no definite conclusions but one: "the data remove the remote possibility of a conspicuous sensitivity of human genes to irradiation." From the outset it had been the consensus of geneticists that the genetic effects

of the bombings would be relatively so small as to be lost in the pathology already prevalent in the population. Failure to detect any increment in pathology therefore gives assurance that, among other things, the genetic effects of radiation are not much greater in man than in experimental animals.

Although the statistics represent over 70,000 pregnancies, the authors have bravely resisted the temptation to extract every plausible inference from their data. Believing that much more research is necessary, they hope that "by refusing to be drawn into premature speculative calculations . . . the geneticist in the long run will arrive more quickly at the goal of a lasting, valid appraisal of this problem."

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DEMOGRAPHIC ANALYSIS: SELECTED READINGS: Edited by Joseph J. Spengler and Otis Dudley Duncan. The Free Press, Glencoe, Illinois, 1956. xvi, 820 pp. $9.50.

POPULATION THEORY AND POLICY: SELECTED READINGS: Edited by Joseph S. Spengler and Otis Dudley Duncan. The Free Press, Glencoe, Illinois, 1956. x, 522 pp. $7.50.

If there are any jaded courses in demography that need a brisk pick-up, help is at hand. In the pair of volumes under review there have been collected no less than 101 articles from professional journals and a few symposia that appeared in the United States, Britain, and Canada between 1928 and 1956. Here, rescued from inaccessibility, if not from oblivion, are a number of highly influential works and some less known that will serve well to stimulate a discussion or illustrate a point. In addition, the editors have supplied a framework of topical divisions, with introductions to each and with supplementary bibliographies.

Whether the volumes may be suitable as "relatively self-contained texts" in courses dealing respectively with demographic analysis and with demographic theory and policy is another matter. For one thing, the material selected falls considerably short of being representative of the full range of the subject. In economic and sociological aspects it may be that it is fairly representative. (More than half the individual contributors are professors of economics or sociology, with the sociologists outnumbering the economists by more than two to one.) But for a subject that inevitably includes elements from many other disciplines, it is a notable lack to have barely represented, or not at all, the contributions of biology, psychology, geography, anthropology, and political science. Another omission is that of excerpts from book-length studies, apart from the United Nations' *The Determinants and Consequences of Population Trends*. Still another is the passing by of almost all studies in other languages and of pre-contemporary works. Finally, the interpretative introductions, critical and suggestive though they are, do not take the place of a fully stated synthesis.

Of the two volumes, *Demographic Analysis* is perhaps the stronger. "As construed in this volume," the editors explain, "the term 'demographic analysis' comprehends not only the statistical manipulation of population data, but more important, the study of such data as a method of solving empirical problems." Primarily methodological or descriptive studies were excluded. The 63 papers have been grouped in seven topical divisions: past and prospective growth and distribution of world population; mortality; fertility, nuptiality, and replacement; international distribution of population and migration; internal distribution and migration; population composition and utilization of human resources (including articles in the field of population genetics by Laurence H. Snyder, Har-

old F. Dorn, Julian L. Woodward, Frederick Osborn, and Otis Dudley Duncan); selected regional studies (including two or three for each continent except North America).

The papers in this volume have been reproduced photographically from the originals in an at first distracting, though in practice quite legible, variety of typographical styles. A more serious criticism is that indication of the place and date of the original publication of each article is given neither in the neighborhood of the text nor in the table of contents. The reader has to search through the acknowledgements to publishers at the front of the book to discover the period to which a particular present tense refers. After performing this labor he may find, for instance, that of the five articles on population genetics, two of the first three, which survey "present knowledge" of the subject, appeared in 1947 and one in 1939. In most of the other topical divisions the range of contemporaneity is as great and its neglect as potentially misleading.

The volume, *Population Theory and Policy*, which, by the way, is well produced, having been reprinted and documented throughout, treats "the implications of demographic phenomena for social structure and for socio-economic change and welfare, . . . [the] development and applications of 'population theory' and . . . [the] policy aspects of population movements." The nine topical divisions, containing in all 38 papers, are entitled: development of population theory; the role of theory in population studies; theory of population growth; population, resources, technology, and levels of living; population and level of economic activity; population growth and international relations; socio-cultural context of population dynamics; population policy.

From the theoretical studies it is difficult to resist the impression of an excessive number of fresh starts on an uphill climb. Not yet have the demographers arrived at a plateau of systematic theory where they can relax on the terrace and admire the view, even halfway up. Such obstacles as the insufficient vocabulary of agreed concepts and the lack of basic data on demographic events in divers cultures and periods persist.

Of the seven articles on policy, three, those by Paul Meadows, Joseph J. Spengler, and P. K. Whelpton, discuss problems of quality explicitly. All consider that qualitative improvement must be a joint aim, along with quantitative controls, in an inclusive policy of enlightenment and welfare. The principal means advocated are making contraceptive aids generally available and providing economic assistance in family formation, as needed.

It is a special merit of both volumes that they succeed in conveying, the greater part of the time, the ferment of lively minds at work and the scruples that guide the profession in dealing with data tempting to vulgarization. A remarkable amount of self-criticism is recorded, along with some museum pieces of unlucky prediction which indicate that something of the kind was in order. For eugenists these volumes will be valuable, not so much for new light on their own specialty as for illumination of the broad foundation of demographic studies on which it rests.

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HEALTH AND DEMOGRAPHY: Halbert L. Dunn; U. S. Department of Health, Education, and Welfare, Public Health Service, Bureau of State Services, National Office of Vital Statistics; Washington, October, 1956, 94 pp., $.50.

In May 1956 the Bureau of State Services of the U.S. Public Health Service conducted a seminar on population dynamics for public health workers. A collection of charts on demography and health topics assembled from Bureau of the Census and

Public Health Service publications for this occasion forms the principal substance of the volume under review. Some 43 charts and one table are presented, grouped in five sections: Dynamics of population trends in the United States; Population trends for major geographic areas and states; Population characteristics: age and marital status; Population characteristics: economic; and Indicators of health and disease.

Each chart occupies a whole page and is faced by a note indicating one or more of its outstanding features. In addition, there is a short paragraph of introduction for each of the five sections. A large proportion of the material refers to 1950 or to changes between 1940 and 1950, but some of the charts go farther back and some, especially in the first section, are carried into the present decade. The volume concludes with a three-page "postscript" by the author giving his views on the proper future orientation of public health research.

This is a welcome publication. Although it does not purport to present information not already available in print, except perhaps for a few "new charts specially prepared" (but not individually identified as as such), it performs a valuable service in bringing together in one place, and at the bargain price of fifty cents, a body of highly interesting and significant material. Not only public health workers but teachers and research personnel in many related fields will be grateful for this convenient compendium.

Since the book was intentionally prepared at minimum cost and depended almost entirely on graphs that were already available, it was not possible to include all topics that might be of interest. Of course one would like to have more recent data on many subjects, but they cannot be charted until they have been collected. If it is for the moment idle to contemplate the day when an up-to-the-minute chart book on public health and demography will appear annually, as does the Historical Supplement to the Federal Reserve Charts, it is to be hoped that new editions of the present collection will appear at least from time to time.

One or two suggestions for the next revision may be in order. In the reviewer's opinion a most important improvement would be to state where the numerical data for each chart can be found. Ideally it would be fine to have a table published in support of each graph, but if that is not possible, a more precise reference than simply the name of the agency that furnished the data would be helpful. This is illustrated by Chart 20, an extreme case that almost merits the comment, made opposite the one set of data given in tabular rather than graphic form, that it is "obviously too detailed to make a meaningful chart" (p. 52). Since the book may well be used by laymen, there might be some value in defining a few terms, such as "labor force" and "birth registration states," inserting a note on problems of statistical accuracy, and drawing explicit attention to each use of a semilogarithmic scale. Many of the brief comments on the charts are so apt that one hopes it may prove possible in a revision to utilize more of the empty space on the pages that they occupy.

The postscript, with its emphasis on the need for discovering the factors that contribute to "positive health," seems quite congenial to some of the ideas of the eugenics movement. Just how and to what extent it will be appropriate to work in this area from a public health approach remains to be determined.

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Social Characteristics of Urban and Rural Communities, 1950: Otis Dudley Duncan and Albert J. Reiss, Jr., John Wiley and Sons, Inc., New York, 1956, XVIII + 421 pp. $6.50.

This volume is one of a series of reports sponsored by the Committee on Census

Monographs of the Social Science Research Council. This Committee was organized in 1950, with the cooperation of the Census Bureau, to stimulate intensive analyses of the 1950 census data on special topics of demographic interest which fall outside the scope of the Bureau's primary services.

The authors, both specialists in the fields of urban sociology and demography, utilize a cross-sectional comparative approach to a vast array of demographic, social, and economic characteristics of American communities in 1950. The conceptual organization is straightforward. The independent variables are conceived to be the community characteristics of size, spatial organization, growth, and functional specialization. The dependent variables are defined as the conventional demographic characteristics of the populations of these communities such as age, sex, race, nativity, family composition, education, income, occupation, and the like. The central organizing hypothesis of the study is that differences by type of community as measured by classifications among the above independent variables are associated with differences in the population composition of the communities. Nevertheless, the authors state that the "study is conceived as an exploration of the research possibilities of a specific body of data, rather than as an effort to develop theory or to check specific experimental hypotheses."

The volume is organized into four sections, each devoted to an analysis of the relationships of a primary independent variable with a number of demographic characteristics. Part I analyzes the demographic differences in communities classified by size. Typical of the research results are findings stated in terms such as—median age varies directly with size of place, the fertility ratio varies inversely with size of place, the per cent married varies inversely, median income directly, and so on. These are illustrative only; the nine chapters comprising Part I treat the entire series of dependent variables systematically. Part II deals with the relationships between the spatial organization of communities and demographic phenomena. One chapter, for example, examines the population characteristics of suburbs and the urban fringe as compared to the central city. Another chapter investigates the effects of urban dominance on rural population characteristics. A similar logic of analysis is pursued in a comparison of metropolitan suburbs with independent cities. Part III examines the compositional differences between urban places which have either rapidly grown or declined over the twenty-year period up to 1950. The twenty-year-old Ogburn hypothesis, that the two factors of increased opportunity and migration constitute the main factors accounting for the differential growth of cities, is tested and generally supported, though not without some substantive and many reservations about methodological differences. Part IV is devoted to determining whether different types and degrees of functional specialization (or principal economic activity) of a community significantly affect its socio-demographic structure. Specializations in manufacturing, trade, education, public administration, transportation, military service, and entertainment and recreation are respectively analyzed in terms of their associated population characteristics.

This study virtually amounts to an encyclopedia of the demographic correlates of the urban-rural "continuum," a concept that the authors repeatedly indicate should be viewed with suspicion. It is admittedly not a comparative study of the sociology of communities; it is not concerned with the internal life or specific social structure of communities, but rather with a comparison of their basic demographic, social, and economic parameters. As such, its main pedagogical use should be as a supplementary source book for advanced students in urban sociology.

Throughout the volume the authors have consistently evidenced imagination in their use and organization of census data and modes of analysis. They have contributed a number of useful classificatory innovations, particularly with respect to community size and functional specialization.

Only one general reservation about the volume seems appropriate. Because of the nature of the comparative analysis, the text becomes a series of associational statements. It would appear that the length of the book might have been substantially reduced by the use of summary tables which verbally described relationships, perhaps in symbolic form.

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THE PSYCHOLOGY OF HUMAN DIFFERENCES: Leona E. Tyler. 2nd Edition. New York, Appleton-Century-Crofts, 1956. pp. VIII + 562.

The accumulation of new information since the first edition of 1947 has compelled a thoroughgoing reformulation. This, then, is a new book. It is written primarily for upper classmen with a definite background in psychology and with some statistical sophistication. Though clearly written, it is not an easy book to read.

In rapid review we survey the *quantitative* findings about individual differences in intelligence, school achievement, vocational aptitudes, personality interests and attitudes, and perception. (The last topic will be new and interesting to those who have not followed current trends in psychology.) There follows a survey of differences found in such groups as those of sex, race, nationality, class, age. Finally there is a discussion of the factors producing the differences.

Readers of this journal will perhaps be most interested in the chapter on intelligence in which some exciting new theoretical possibilities are briefly set forth, and in the last part dealing with the relationship between hereditary and environmental influences. Like all competent scholars, Tyler recognizes that the question is wrongly stated in terms of hereditary *or* environment, nature *versus* nurture. The causal factors of psychological characteristics are, of course, *interactive*. The most usable question about any psychological characteristic is "not the relative proportions of hereditary and environment in its make-up, but how amenable it is to change, and under what circumstances we can expect changes to occur. . . . Hereditary tendencies can often be strikingly modified. Environmentally produced traits are often so firmly fixed that it is impossible to shake them." (p. 449) Useful, if not completely conclusive, evidence is marshalled bearing on these questions: "(1) *How much* difference can we expect a change of environment to make in the kinds of traits that have interested . . . [us?] (2) *which* environmental conditions are the ones that really count most heavily in psychological development?" (p. 450)

One significant conclusion is that environmental influences affect the central tendency of the group being studied more than they do its variability. Improvement in environment does not wipe out differences or produce uniformity. Thus the differential psychologist is warranted in his insistence that the proper study of mankind is not only "man" but "men."

Tyler's review of dysgenic or eugenic factors in population trends is brief. Even so, she finds it too hot to handle. The problem exists, but at present no simple statement about these trends is adequately supported. Yet we dare not give up, for the most important natural resource for us to conserve is human quality.

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PERIODICAL REVIEWS

GENETICS

The heterozygous and homozygous manifestation of certain metabolic disorders. U. Pfändler. *Journal de Génétique Humaine* **5** (1956), pp. 248-260.

New findings in three hereditary metabolic diseases seem to reveal carrier states. In a family with a rare form of chronic porphyria the possible carriers excreted abnormal quantities of porphyrin pigment. In two families afflicted with cystinuria, a general increase in amino acid excretion was found in some of the younger relatives but not in all the presumed adult carriers. In two families with Niemann-Pick's Disease the relatives taken all together showed an elevation of both fatty acids and phosphorus in the blood. The author suggests that chemical defects are more likely than anatomical defects to present "microsymptoms" in genetic carriers.

A note on the future of phenylketonuria. J. E. Cawte. *Journal of Mental Science* **102** (1956), pp. 805-811.

It now appears to be within the power of medicine to detect all cases of phenylketonuria soon after birth and to prevent the usually resulting mental defect. However, this would entail such a cruel distortion of dietary habits of affected children that their mental and emotional problems might become a greater evil than mental defect itself. If such individuals do grow up to have children, the frequency of the gene will multiply, and if they marry their own kind, as deaf marry deaf, the frequency of the manifest disease will be greatly increased. Since phenylketonuria is genetically simple and clinically well defined, the author urges the adoption of public health measures to control the disease either by withholding treatment or by sterilizing those treated.

The genetics of human behavior. F. J. Kallmann. *American Journal of Psychiatry* **113** (1956), pp. 496-501.

The essential role of heredity in mental development is now generally recognized among behavioral scientists, even though many call it by other names. It is agreed that each individual responds to different aspects of the environment in a sequence determined biologically, that different individuals may be influenced by different aspects of the same environment, and that some children cope successfully with situations that would be too traumatic for other children. Self-determination in development is well illustrated by identical twins. If much of the resemblance in such twins stems from early environmental similarity, then the environmental similarity itself demonstrates the degree to which children select or shape their own environment. In order to plan his own future as well as he plans that of the world around him, man must gain a better understanding of heredity-environment interactions in his own development.

Fertility and blood groups of some East Anglian blood donors. J. H. Bennett and C. B. V. Walker. *Annals of Human Genetics* **20** (1956), 299-308.

Although abortions due to blood incompatibility may be more frequent in mothers of certain blood groups, this does not necessarily lower the fertility of these mothers. The authors observed a suggestive excess

of complete childlessness among married women of blood groups A and B, but found no fertility differences that could be attributed to higher fetal death rates in any blood group. Variability of family size was found to be much greater than expected by chance. Reproductive differentials may therefore still be a potent force of natural selection in civilized man.

The relationship between the occupational status of individuals and the sex ratio of their offspring. H. L. Fancher. *Human Biology* **28** (1956), pp. 316-322.

The proportion of male children in a family is not affected by masculinity of the parents as expressed in their occupation. Analysis of "Who's Who in America" and of "Who's Who Among American Women" failed to confirm the earlier reports of Bernstein that parents in masculine occupations have more male children, or that the first two children in a family are of the same sex more often than expected by chance. The study did give significant evidence that parents with two children of like sex are more likely to have another child than those with two children of opposite sex.

Heredity in rheumatic fever. Some later information about data collected in 1950-51. A. C. Stevenson and E. A. Cheeseman. *Annals of Human Genetics* **21** (1956), pp. 139-144.

In 462 families of Belfast, Ireland, containing at least one member with rheumatic fever, the proportion of affected children was too low in 1951 and is still too low to conform to a simple Mendelian pattern of heredity. These results contrast with those of Wilson and others in America, where the frequency of rheumatic fever closely approached the expected level for a simple recessive disease even before all children had passed through the age period when there is risk of onset.

An investigation of the frequency of consanguineous marriages among the Mormons and their relatives in the United States. C. M. Woolf *et al. American Journal of Human Genetics* **8** (1956), pp. 236-252.

In recent years, over most of the United States, about one in 2,000 marriages has been between first cousins. A century ago the frequency was about one in 200, with frequencies as high as 3 or 4 per cent in such areas as rural North Carolina. Recent reports from other countries range from two per thousand in part of Ireland to 13 per cent among the Indian Parsees. Although Mormons, like many religious groups, favor endogamous marriage, inbreeding is not significant among them. In an investigation of 198 marriages between persons with a common surname, only two were possibly between first cousins.

Studies on irradiated populations of Drosophila melanogaster. B. Wallace. *Journal of Genetics* **54** (1956); pp. 280-293.

After nearly 150 generations of continuous exposure to radiation and natural selection, fruit flies show little or no loss of biological fitness. Maintained in crowded cultures, the populations achieved genetic equilibrium with a load of recessive or hidden lethal mutations about four times that in an unirradiated control population. Evidently, many mutations that are lethal in double dose were successfully incorporated in single dose into favorable gene combinations instead of being eliminated. It seems that much of evolution may depend on mutations with beneficial dominant effects and deleterious recessive effects.

The genetical consequences of assortative mating. E. L. Breese. *Heredity* **10** (1956), pp. 323-343.

Mating of unrelated individuals who are similar with respect to a measurable character increases the proportion of extreme types in a population without reproducing the defects of inbred lines. Both

theory and plant experiments show that assortative mating continued for generations widens the differences among families without greatly increasing the number of homozygous individuals. Inbreeding increases family differences by bringing together identical genes; within lines it tends to produce uniformity for all traits and to diminish vitality. Assortative mating brings together different genes having similar effects; it preserves variability within families in traits not involved in the mating pattern and maintains nearly normal vitality.

Causes of congenital myxedema and the genetic aspects of thyroid disease. M. Bernheim, *et al. Journal de Génétique Humaine* **5** (1956), pp. 225-247.

Partial or total atrophy of the thyroid gland from birth, congenital myxedema, appears to be usually a recessive hereditary disease, and the responsible gene may be detected in heterozygous or carrier relatives by major or minor thyroid dysfunction. Fifty children with myxedema dating from the first two years of life were studied together with their families. There was a high incidence of thyroid disease in the family histories, but only one mother had clinical thyroid disorder in the pregnancy which produced the affected child. When tested with radioactive iodine, 35 parents and 24 siblings with no symptoms of thyroid disease nearly all showed thyroid activity above normal.

The hypothesis of recessive inheritance is not satisfied by the small observed number of affected siblings unless nine unexplained early deaths in siblings were cases of the disease. The authors suspect that, in addition to the genetic factors, an abnormal placental barrier may be required for a gestation to end in congenital myxedema.

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POPULATION

Eugenic sterilization. James B. O'Hara and T. Howland Sanks. *Georgetown Law Journal* **45**, 1 (Fall, 1956), 20-44.

Two articles in a series of studies on population by the Social Science Department of Loyola College of Baltimore have appeared in *Eugenics Quarterly* (**2** [Sept., 1955], 140-151, and **3** [Mar., 1956], 9-15). This third article presents a survey of the legal history and status of sterilization in the United States, giving brief mention to therapeutic and contraceptive sterilization and focusing on eugenic and punitive sterilization.

In the state courts, it now appears that sterilization is not a cruel and unusual punishment; nor, even when applied only to inmates of state institutions, a denial of equal protection of the laws; nor, where notice and hearing are provided, a violation of procedural due process of law, though there is some disagreement about requirements with respect to appeal. The United States Supreme Court has decided only two sterilization cases. In *Buck v. Bell* (1927) the Court held that substantive due process of law was not violated by an order to sterilize an imbecile whose mother and daughter were also imbeciles. The decision in *Skinner v. Oklahoma* (1942), in contrast, struck down an Oklahoma statute providing for sterilization of a person thrice convicted of a felony involving moral turpitude, on the ground that the Court had no basis for inferring that the line distinguishing persons subject to the law from other criminals had any significance in eugenics or heredity.

Sterilization laws, most of which apply exclusively to inmates of state institutions, are now in effect in 28 of the 33 states and territories that have at one time had such laws. The number of eugenic sterilizations reported has dropped from 9,200 in 1941-1945 to 6,100 in 1951-1955. This decline,

which the authors believe will continue, is attributed to a conservative report on eugenic sterilization by the American Neurological Association, the abuse of sterilization legislation in Nazi Germany, recent studies in heredity, the influence of the Roman Catholic Church, and changed legal thinking.

To their very convenient and useful summary of the legal situation the authors have added two passages (pp. 29-32, and 40) in which they take issue with the reasoning of the courts and indicate the direction of their own thinking.

Population policies in Communist China. Irene B. Taeuber. *Population Index* **22,** 4 (October, 1956), 261-274.

The official census-registration figures for the Chinese population as of mid-1953 showed a total of 602 million persons, of whom 583 million were said to be residents of Mainland China, a number considerably in excess of many of the rough guesses demographers have made of the size of this large segment of the world's population. Further, a growth rate of about 2 per cent per annum was reported. If the rate of increase is actually of this order, it poses serious problems for advances in industrialization, consumption levels, and education.

The article under review summarizes the available evidence as to Chinese Communist thinking on the population question. It appears that a substantial movement toward encouraging family limitation is under way. This is being accomplished without abandonment of the Marxian position that high growth rates are no threat to the national economy as a whole. Emphasis is placed on the protection of the health of women and children for the purpose of permitting study and work for the realization of the new order.

The means by which family limitation is to be achieved is apparently intended to be voluntary "birth control." This phrase includes abortion and sterilization, as well as contraception, among its meanings, and there is some indication that restrictions on these two practices are being relaxed. Meanwhile the broader framework of population policy includes encouragement of migration to the sparsely settled border areas, and direct assaults on the family system and the ancient role of women.

Whether fertility can be lowered significantly remains to be seen. Shortages of health personnel and facilities are already severe, but the reaction of the traditional rural society to pressures for family planning is less predictable than it once seemed. In the absence of economic collapse, it is to be expected that the Chinese population will grow much larger. Hence "it is probable that there will be firmer and more comprehensive campaigns for reducing family size in future years" (p. 273).

A note by the author and Leo A. Orleans on the population statistics of Communist China follows the main article (pp. 274-276).

A demographic study of a Dinka village. D. F. Roberts. *Human Biology* **28,** 3 (September, 1956), 323-349.

The demographic position of the Dinka village of Tir in the southern Sudan early in 1954 is described and discussed in this article on the basis of information obtained by direct observation. Family relationships were determined by getting to know the individuals by sight and name. Ages were estimated on the basis of dental condition, remembered events, and, for males, the formal age-set system; and from comparison of individuals not classified by these means with those who were.

Of the 375 individuals, 48 per cent were younger than 15, the mean age being about 20. All the males over 30 and all females over 20 had been married, the average age at first marriage being estimated at 27 and 18, respectively, for the two sexes. On the basis of questioning, an estimate of 5.1 live

births per woman living through the reproductive period was obtained, a figure that the author believes to be "markedly affected by the spacing of children, regarded as socially desirable" (p. 341). [No information is given as to how this spacing was achieved.] The possible depressing effect on fertility of the observed excess of females over males in the reproductive ages is restrained, but not entirely overcome, by some polygamy and by the practice of the levirate. Whether the population is growing the author finds difficult to decide, but he concludes that it is.

> "The possibility of genetic drift occurring . . . is shown by examination of the mating pattern to be remote, while the demographic situation is such as would be conducive to the operation of natural selection" (p. 348).

Some comments on birth, death and infant mortality rates in the Philippines, and a suggested device for registration improvement. Frank S. Morrison. *The Philippine Statistician* **5**, 2 (June, 1956), 98-105.

An attempt to throw some light on the vital rates of the Philippines is made in this article through the division of the country into two categories: (1) cities and provinces with rates significantly below the national averages, and (2) remaining cities and provinces. The 1954 crude birth and death rates per thousand for the former were 22.5 and 8.3, respectively, while for the latter they were 39.5 and 11.7. On the assumption that even the areas with higher rates are subject to some underregistration, the author suggests that the actual birth rate was about 45 and the death rate about 13. A similar analysis leads to an estimated infant mortality rate of 92 deaths per thousand live births.

The author points out one difficulty of such an analysis, the uncertain quality of the 1954 total population estimates used as bases for the rates. These figures were calculated by the Bureau of Health by assuming constant after 1948 the average annual population increases observed between the 1939 and 1948 censuses. Another problem the reviewer would like to have seen discussed is the possibility that the differentials shown by the areas with low rates may have been in part genuine and not simply the result of underregistration.

The device suggested for registration improvement is the establishment of registration areas for the several vital rates, followed by concentrated effort to raise the quality of the statistics in the regions not initially admitted to the areas.

The Netherlands-Canadian migration. A. S. Tuinman. *Tijdschrift voor Economische en Sociale Geografie* **47**, 8 (August, 1956), 181-189.

Some of the aspects of an overseas movement since World War II of more than 100,000 persons are discussed in this article by the Dutch official who was Netherlands Agricultural and Emigration Attaché in Canada from 1946 to 1956. Operating under an informal agreement between the two countries, and subsidized by the Netherlands but not by Canada, this selective migration has accounted for about 45 per cent of post-war Dutch emigration and something of the order of 10 per cent of Canadian immigration.

Initially heavily weighted toward agriculturists, the occupational composition of the migrants has become much more varied since 1951, when admission restrictions were made less stringent. As compared with all immigrants to Canada, the Dutch have settled much less in Quebec, somewhat more in the Maritime Provinces and Ontario, and in about the same proportion in the western provinces, with a particularly heavy concentration around Edmonton. Interviews by the author and his staff with immigrants are the basis for the conclusion that "integration of Netherlanders in Canada is proceeding satisfactorily" (p. 186). Several ways in which the success of

future migration might be furthered are suggested, including stabilization of the admission regulations and various forms of improved subsidies, credit facilities, and social security plans.

A substantial portion of the article is devoted to strong disagreements with Petersen's *Planned migration: the social determinants of the Dutch-Canadian movement* (University of California Press, 1955) as to both the bases and the results of the movement under study. Readers will find the differing interpretations of the two authors interesting to compare. One subject on which the reviewer would like to have seen more extensive comment in the article is the reasons for the pro-emigration policy of the Netherlands government.

A bonanza for industry—babies. *Newsweek*, January 4, 1957, pp. 32-34.

The reviewer would like to call attention to this article as a generally excellent popular report of demographic findings that is marred by serious defects.

The main point of the article is that large population growth is to be expected in the United States in the next two decades, with important effects on the demand for various goods and services. Furthermore, as a result of recent fertility history, the growth of the labor force will not precisely parallel that of the total population on a year-to-year basis, a fact that will lead to special problems.

All this is important. It is cogently presented, with illustrations that should bring home the implications of present population trends.

What should make many demographers uneasy is the air of certainty that is carried over from highly probable general statements to specific predictions: "The U. S. *will* . . . reach 200 million sometime in 1967" (p. 32, italics added). Perhaps so, but it cannot be demonstrated now.

Not until the very end of the article is it mentioned that the analysis is based on only the highest of three Bureau of the Census projections of the population, and then with the unwarranted implication that there is no possibility that the growth prospects have been overestimated. (In this connection, readers may wish to compare the article under review with the same journal's own interview with P. K. Whelpton in the issue of July 13, 1956, especially pp. 84-85). As demographers become increasingly aware of the need for modesty about their ability to foresee the future, it is unfortunate to perpetuate in the public mind the idea that population projection techniques are more dependable than they really are.

Page 33 contains some inexcusably distorted graphs, in which increases of 36 per cent, 65 per cent, and 48 per cent appear to be about 300 per cent, 200 per cent, and 200 per cent, respectively.

GEORGE F. MAIR
Smith College

NEWS NOTES

Meetings

The Population Association of America held its annual meeting at the University of Pennsylvania, May 4 and 5, 1957. Applications of demography were discussed in economic analysis; public administration and business; fertility and nuptiality; urban, rural, and regional analysis; morbidity and mortality. The United States population for 1975 was reported on according to size, age, and sex composition; color and nativity; regional and urban-rural distribution; size and distribution of cities; the labor force. Current demographic research programs were discussed.

The American Society of Human Genetics conducted its tenth annual meeting with the American Association of Physical Anthropologists at the University of Michigan, April 12-14, 1957. The emphasis of the joint meeting was upon the relation of genetics and anthropology. Sessions were held on the anthropology of the skeleton, anthropology and genetics, anthropology and human genetics, physical anthropology, natural selection in man, and medical genetics.

The following officers were elected for 1958: Madge T. Macklin, President; Frederick Osborn, Vice President; H. W. Kloepfer, Treasurer. James F. Crow, Paul R. David, and E. R: Dempster were elected directors.

The National Council on Family Relations will have its annual meeting at Purdue University, August 21-27, 1957. The theme of the meeting will be "Intercompetence and Family Living: An Interprofessional Approach."

Research

Mental Illness: Some 10 per cent of the Baltimore population are at one point mentally ill, excluding those in institutions, reports the Commission on Chronic Illness, according to preliminary data from an illness survey. This estimate of mental illness may hold true for the country as a whole. Baltimore is similar to other cities in family income and age distribution, except for a non-white population of 27 per cent which tends to lower rates.

We doubt very much that a population having more than this rate of mental illness, in addition to the heavy load of chronic and acute disease found in the Baltimore survey, could function as a society, the report asserted.

Psychoneuroses were twelve times as common as the psychoses. Male psychoses were twice as frequent as psychoses in women, but women had more psychoneurotic and psychophysiological disorders. Impairment in such disorders, however, was insignificant or mild. The psychoses rose sharply with age.

Ability and College Attendance: Sheer level of ability, a good predictor of whether a student plans to go to college, is an even better predictor of whether he will actually go. The higher the ability level, the larger the per cent of students planning to go, and of those planning to go, the larger the per cent who actually do go. Moreover, the higher the ability level, the larger the per cent of those not originally planning to go who nevertheless do attend college. At all levels of ability, the per cent of girls who carry out their intentions to go to college is lower than for boys. These findings are reported by John W. French of Educational Testing Service.

Publications

Population Review, a new journal, is being published by the Indian Institute for Population Studies in Madras. Professor S. Chandrasekhar is Editor. Volume I began with January 1957.

THE X INTERNATIONAL CONGRESS OF GENETICS

The X International Congress of Genetics will be held at McGill University, Montreal, Canada, from August 20-27, inclusive, 1958. Congress Committees are now actively preparing for your arrival and raising funds for travel grants, particularly for overseas geneticists.

The program will include symposia, invited papers, short contributed papers, demonstrations, other meetings and exhibits. There will be a special exhibit on "The Role of Genetics in the Service of Man." Also, we are preparing an interesting program for the ladies and children and the latter will be card for in a "Progeny Park."

Pre- and post-Congress tours both local and extending through eastern parts of Canada and the United States are being arranged. University residences, hotels, tourist homes or camping facilities can be arranged for members and their families.

Overseas transportation should be arranged very soon as travel accommodation is already being heavily booked for 1958. Family travel plans should be investigated.

If there is any possibility that you will be able to attend, we ask you to fill in the information requested below and send it to us *immediately*.

THE SECRETARY GENERAL

Professor J. W. Boyes,
Department of Genetics,
McGill University,
Montreal 2, P.Q., Canada.

Please send me further information regarding the X International Congress of Genetics.

Name: (please print) _____

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PRINTED MATERIALS

SPRING-SUMMER, 1957—Reprints, Pamphlets• at 25¢ a copy.

SPECIAL SERIES: **Radiation and Genetics**

Genetics in the Atomic Age, Curt Stern

Estimation of Spontaneous and Radiation-induced Mutation Rates in Man, James F. Crow

GENERAL EUGENICS

Galton and Mid-Century Eugenics: The Galton Lecture, 1956, Frederick Osborn

Research on Intelligence and Personality (Committee Report, American Eugenics Society)

Fertility Control in the Light of Some Recent Catholic Statements, Parts I and II, Wm. J. Gibbons, S.J.

European Heredity Registers, Jan A. Mohr

Present Status of Research on Populations, Frank A. Lorimer

Dynamics of Human Populations, Dudley Kirk

Genetic Aspects of Population Replacement, Frederick Osborn

Relation of Population Changes to Distribution of Genetic Factors: World Population Conference Report

Tested Intelligence and Family Size, Anne Anastasi

Future Fertility of American Women, P. K. Whelpton

Female Sterilization in Puerto Rico, J. Mayone Stycos

Effects of Differential Fertility on Genetic Endowment, Frederick Osborn

Heredity and Learning Ability in Infrahuman Mammals, J. P. Scott

Trends in Capacity for Intelligence, Frank A. Lorimer

Address of Pope Pius XII to Primum Symposium Geneticae (1953)

Effect of Birth Control on Intelligence and Character of Succeeding Generations, Frederick Osborn

EUGENICS AND HEALTH

Genetic and Eugenic Aspects of Early Total Deafness, Diane Sank and Franz J. Kallman, M.D.

Hereditary Susceptibility in Rheumatic Fever, May G. Wilson, M.D.

Treatment in Hereditary Diseases, Bertha M. Aschner, M.D.

Influence of Heredity on the Health of the Family, Barton Childs, M.D.

Heredity and Diabetes, Arthur Steinberg

Heredity and the Eye, Conrad Berens, M.D.

Heredity of Joint Diseases, Robert M. Stecher, M.D.

Eugenics and Preventive Medicine, C. Nash Herndon, M.D.

EUGENICS AND THE FAMILY

Psychiatry and Marital Problems, Emily Mudd

Education for Personal and Family Living, Frederick Osborn

•Heredity Counseling: Its Services and Centers, Helen G. Hammons

Scandinavian Family Allowances, Halvor Gille

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Sex Education and Eugenics, Jacob Goldberg

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Family Allowances in Brtain, Canada, Australia, New Zealand, R. Chambers

International Family Legislation, Helen G. Hammons

Contribution of Planned Parenthood to the Future of America, Frederick Osborn

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BACK ISSUES—EUGENICS QUARTERLY, Volumes 1 to 3 (1954-1956) and EUGENICAL NEWS, Volumes I to XXXVIII 1915-1953) available.

1957: EUGENICS QUARTERLY, Volume IV—Journal of the American Eugenics Society. 64 pages; population, genetics, reviews, etc. $3.00 a year,. *sample copy free.*

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Manuscripts: One original and one carbon should be submitted, typewritten and double-spaced. Legends for figures and plates should be typed and clearly marked on separate sheets.

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> Fuller, J. L., & Scott, J. P. 1954. Heredity and learning ability in infrahuman mammals. *Eugen. Quart.* 1: 28-43.

Abbrevations for titles of medical periodicals should conform to style adopted by the Armed Forces Medical Library, as published in the *Index-Catalogue of the Library of the Surgeon General's Office*, Fourth Series, Vol. 10.

Proofs: Galleys will be sent to author for his correction with reprint orders. One hundred reprints supplied free to each author.

THE EUGENICS REVIEW

Volume 49 APRIL 1957 Number 1

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TWIN RESEARCH IN TUBERCULOSIS — BARBARA SIMONDS

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Dudley Seers:	A Fertility Survey in the Maltese Islands.
A. Peacock:	Review Article.

Book Reviews:

List of Books and Publications Received.

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